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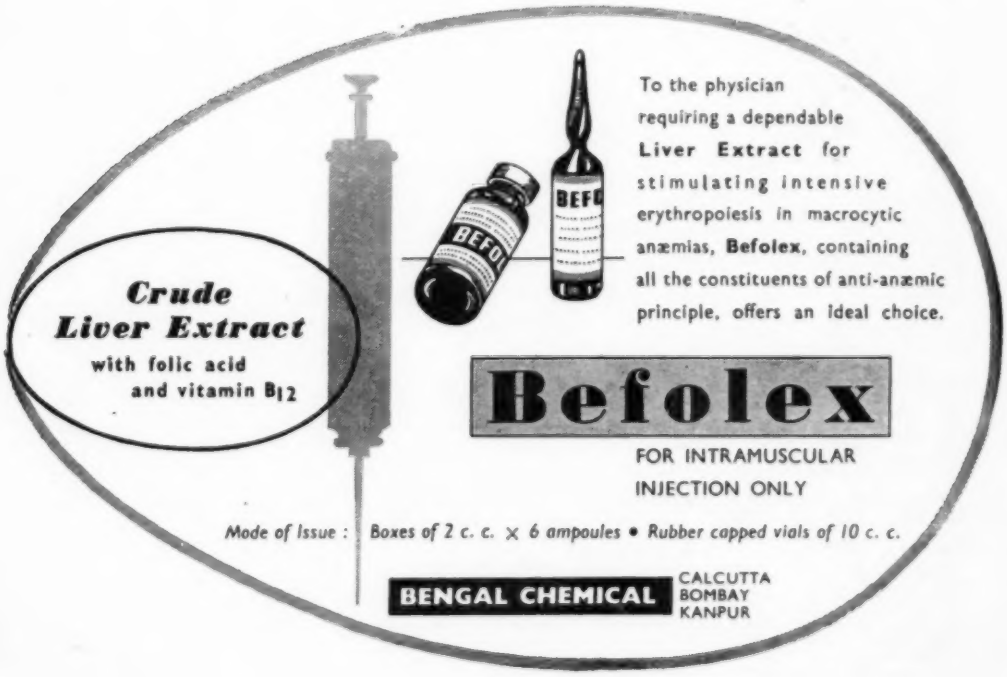
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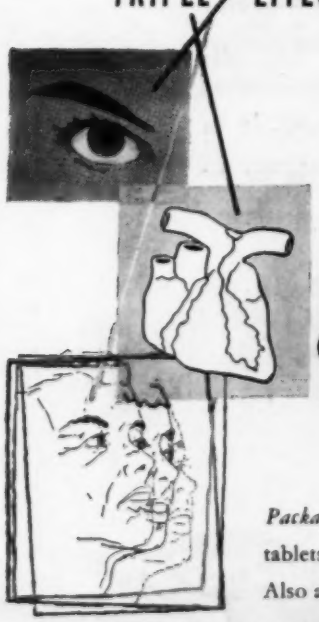

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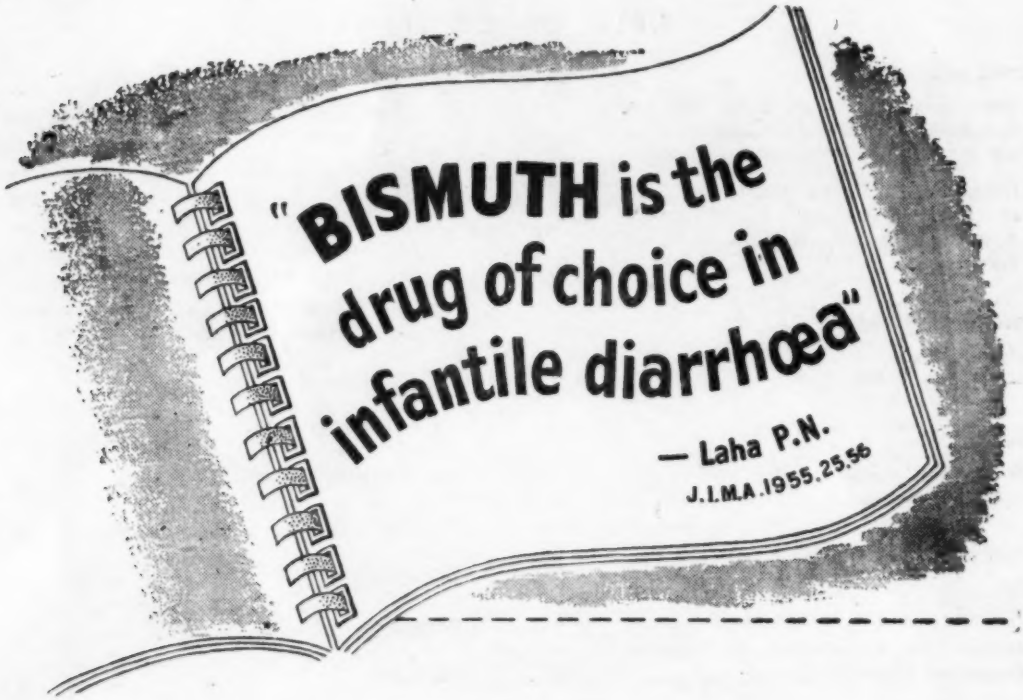

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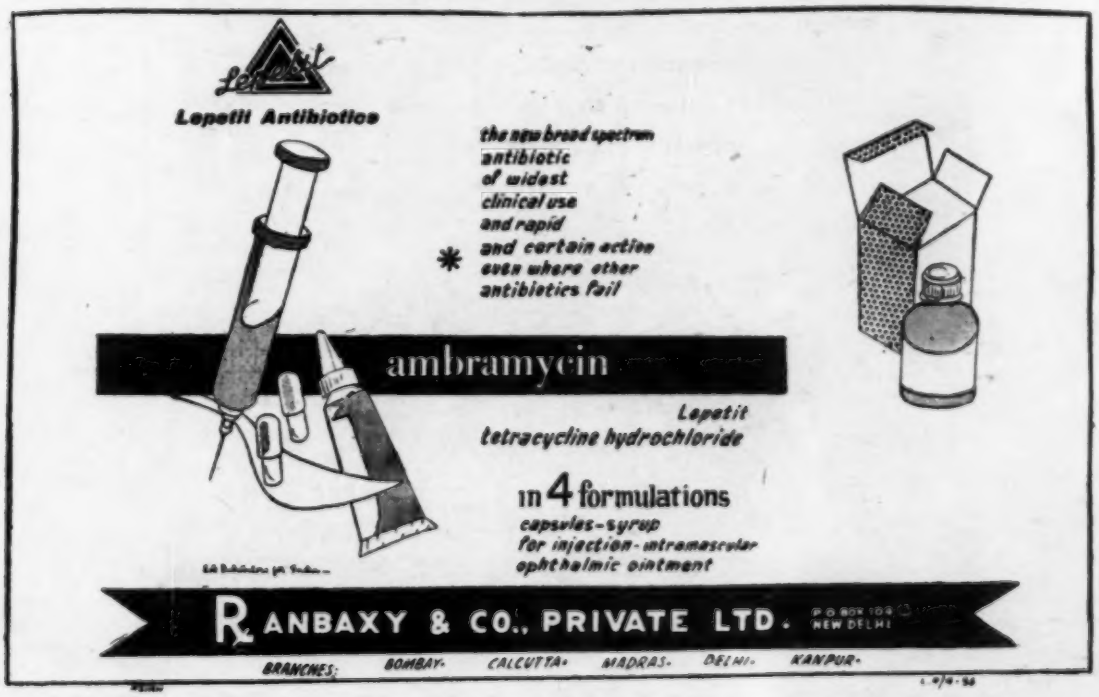

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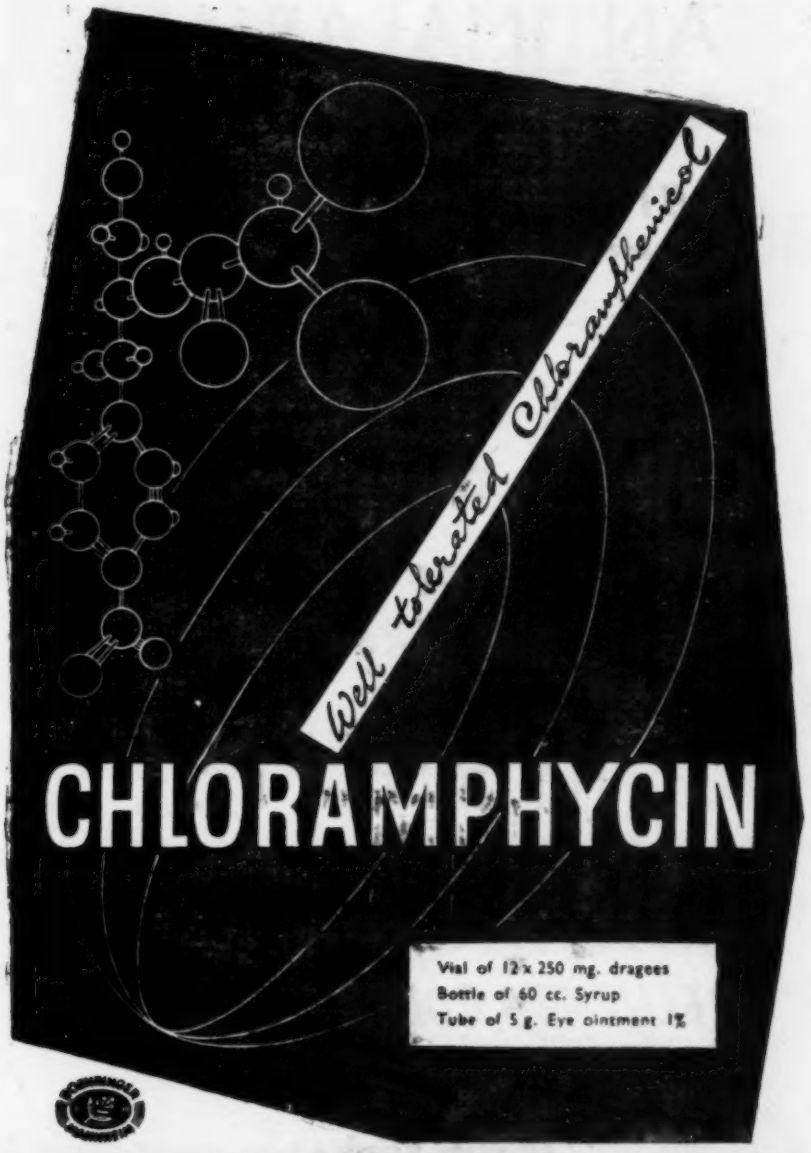

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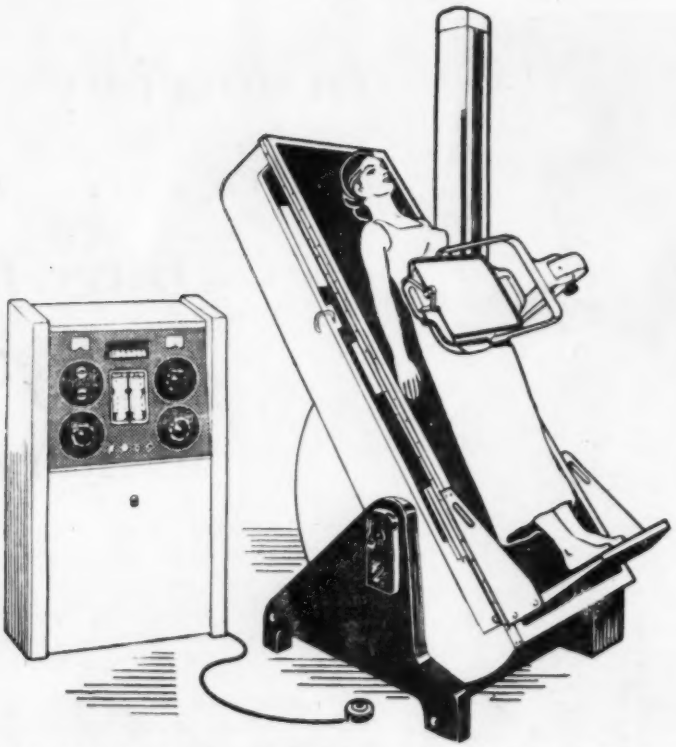

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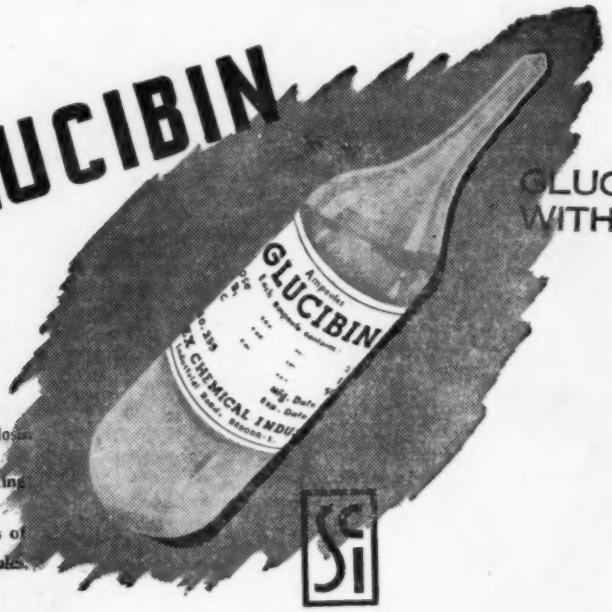

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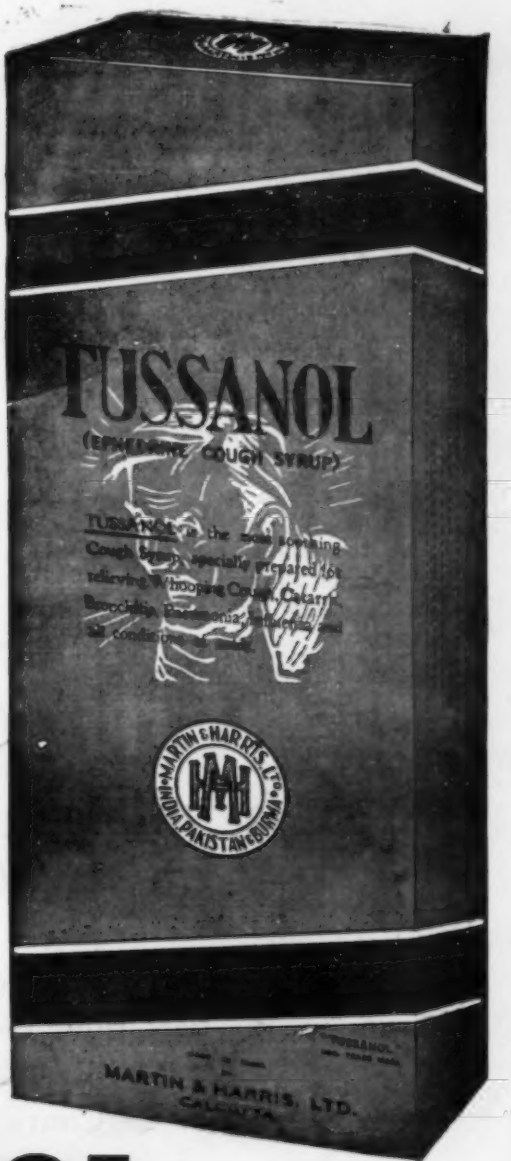

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Journal of the Indian Medical Association

VOL. 27, No. 5 — CALCUTTA — SEPTEMBER 1, 1956

PUBLISHED TWICE A MONTH

ORIGINAL ARTICLES

ANTIBACTERIAL EFFECTS OF SOME SYNTHETIC COMPOUNDS ON *V. CHOLERAE* AND OTHER ORGANISMS

S. C. LAHIRI, M.D.,

Department of Medicine,

AND

A. C. GUHA, M.B., B.S., D.BACT.,

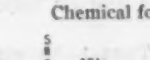
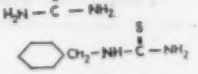
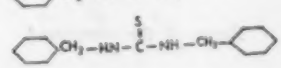
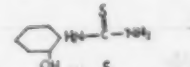
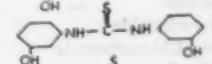
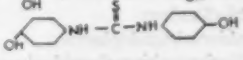
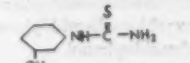
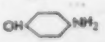
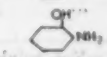
Department of Pathology and Bacteriology,

Calcutta National Medical Institute and Chittaranjan Hospital, Calcutta.

In an earlier investigation Lahiri (1949) and Lahiri and Dutta (1949) reported the antibacterial effect of a 'crude drug' named thiodiamine, obtained from the decomposition products of the barks of *Crataeva roxburghii* (Bengali syn : Barun), and also of *Moringa pterygosperma* (Bengali syn : Sajina), on the *V. cholerae in vitro*, and *in vivo*, when administered orally in cholera patients. The results prompted us to proceed with further investigations with allied chemical compounds. With the use of the compound N'N' dibenzyl-thiocarbamide, the synthetic thiodiamine (Chakravarti, 1951), the original findings with the crude drug could not be corroborated. This anomaly may be explained by the fact that probably thiodiamine in the 'crude extract' contained some principle or principles, possibly of the nature of one of the compounds discussed below, which were lost in the finer synthetic assemblage of the compound. This new synthetic compound is chalky white in colour while the original 'crude' drug was cream coloured. It may be mentioned here that most of the compounds discussed below were brownish in colour.

In the present series, the effects of ten new compounds, generally of phenyl and diphenyl linkages, were tried on different bacteria. The compounds showing inhibitory action on the *V. cholerae* were selected out and their inhibiting powers were tested to higher dilutions These compounds were then tested in *vivo*. The details of the procedures and results of clinical trial of some of them are recorded here.

COMPOUNDS TESTED AND THEIR FORMULAE

Compounds	Chemical formulae
Thiocarbamide	
Benzylthiocarbamide	
N-N-Dibenzyl-thiocarbamide (thiodiamine)	
Orthothiocarbamidophenol	
3'-3'-Dihydroxythiocarbamidophenol	
4'-4'-Dihydroxythiocarbamidophenol	
Metathiocarbamidophenol	
Para-aminophenol	
Ortho-aminophenol	
Paracarbamide	

Methods

Solubility of the compounds—This was tested in cold and in warm water. The compounds which did not dissolve in either cold or warm water were boiled. The insoluble ones were suspended in gum acacia for the purpose of *in vitro* investigations. The solutions of some of the compounds became coloured and the changes have been noted against their respective names in Table 1.

The mother solutions or suspensions were prepared in the peptone water media. The reactions of these solutions or suspensions were then tested against litmus paper. Results are shown in Table 1.

The mother solutions were then diluted in equal amounts of alkali peptone medium from a range of 1/500 to 1/32,000 or more, by series of double dilutions. Similarly, the compounds in suspension were distributed in different test tubes to have similar dilution ranges. The same method was applied in cases of other media also.

Test in vitro—Inoculation was made with approximately 1 million organisms, per 10 c.c. of medium, from a 24-hour subculture of the different test organisms. Controls were kept for both the soluble and insoluble series. pH of the media varied initially from 7·4 to 8·4, according to the test organisms. Results were observed after 24, 48, and 72 hours' incubation, at 37·5°C. The solutions showing no growth after incubation for 72 hours, were further confirmed by culture on solid medium. This was done by inoculating respective dilutions, after 72 hours' incubation, on taurocholate agar media in cases of *V. cholerae* and on solid agar plates in cases of others. The surface of the plates was divided into triangular areas and a drop of the different dilutions of the compounds showing no growth after 72 hours' incubation was placed on the surface of the medium inside the triangular areas. The plates were incubated and the results noted (Tables 2 and 3).

From the above observations it was found that the effects of ortho- and 4′4′ dihydroxythiocarbamidophenol compounds were more pronounced against *V. cholerae* than others. Ortho showed inhibition of growth in both liquid and solid media upto a dilution of 1/32,000; and 4′4′-dihydroxy compound showed inhibition upto a dilution of 1/40,000. Subsequently two other compounds—ortho-aminophenol and para-aminophenol—were also tested and showed inhibition of *V. cholerae* in dilutions upto 1/60,000 and 1/50,000 respectively. All these four compounds were selected for clinical trial.

Test in vivo—Before undertaking the clinical trial of the above mentioned compounds, two of them, e.g., ortho- and 4′4′ dihydroxythiocarbamidophenol, were subjected to further tests for determining the toxic effects, if any, on healthy rabbits weighing more than 1000 g. A rubber catheter with a glass funnel attached to one end was used for introducing the compounds into the stomach of the rabbits. The catheter was introduced through the mouth after immobilising the rabbits by mechanical means. Initially 30 mg. of the substance per kg. body-weight was introduced with minimum amount of water and this dose was repeated every four hours, for 12 hours daily, for two days. The animals were

Table 1—Showing Physical and Chemical Characters and Toxicity of the Compounds

Name of the compound	Solubility in water			Suspension with acacia	Colour of the solution	Reaction against litmus paper after mixture with peptone water	Toxicity against rabbits
	Cold	Warm	Boiling				
Thiocarbamide	−	−	−	Emulsion	Greenish yellow	Slightly acid	...
Benzylthiocarbamide	−	−	+	...	...	No change	...
N-N-dibenzylthiocarbamide (Thiodiamine) ...	−	−	+	...	Deep brown	Slightly acid	...
Orthothiocarbamidophenol ...	−	−	+	...	Greenish yellow	Acid	Very low
3′-3′-dihydroxythiocarbamidophenol	−	−	+	...	Light brown	Slightly acid	...
4′-4′-dihydroxythiocarbamidophenol	−	−	+	...	Port wine	Acid	Very low
Metathiocarbamidophenol ...	−	−	+	...	...	Acid	...
Paracarbamide	−	−	+	...	Port wine	Slightly acid	...
Para-aminophenol	−	−	+	...	Light brown	Slightly acid	Very low
Ortho-aminophenol	−	−	+	...	Light brown	Slightly acid	Very low

− =Not soluble + =Soluble ... =Not tested or observed or recorded.

TABLE 2—SHOWING EFFECTS OF THE COMPOUNDS ON *Vibrio cholerae*

Name of compound	No. of hours observed	Dilutions of compounds used in media												Remarks
		1/1000		1/2000		1/4000		1/8000		1/16000		1/32000		
		L.M.	S.M.	L.M.	S.M.	L.M.	S.M.	L.M.	S.M.	L.M.	S.M.	L.M.	S.M.	
Thiocarbamide ...	24	+	+	+	+	+	+	+	+	+	+	+	+	
	48													
	72													
Benzylthiocarbamide ...	24	−	−	−	−	+	+	+	+	+	+	+	+	
	48	−	−	−	−									
	72	−	−	−	−									
N′-N′-Dibenzylthiocarbamide ...	24	+	+	+	+	+	+	+	+	+	+	+	+	
	48													
	72													
Orthothiocarbamidophenol ...	24	−	−	−	−	−	−	−	−	−	−	−	−	
	48	−	−	−	−	−	−	−	−	−	−	−	−	
	72	−	−	−	−	−	−	−	−	−	−	−	−	
3′-3′-Dihydroxythiocarbamidophenol ...	24	−	−	−	−	−	−	−	−	+	+	+	+	
	48	−	−	−	−	−	−	−	−					
	72	−	−	−	−	−	−	−	−					
4′-4′-Dihydroxythiocarbamidophenol ...	24	−	−	−	−	−	−	−	−	−	−	−	−	Upto 1/40000
	48	−	−	−	−	−	−	−	−	−	−	−	−	
	72	−	−	−	−	−	−	−	−	−	−	−	−	
Metathiocarbamidophenol ...	24	+	+	+	+	+	+	+	+	+	+	+	+	
	48													
	72													
Paracarbamide ...	24	−	−	−	−	−	−	−	−	−	−	+	+	
	48	−	−	−	−	−	−	−	−	−	−			
	72	−	−	−	−	−	−	−	−	−	−			
Para-aminophenol ...	24	−	−	−	−	−	−	−	−	−	−	−	−	Upto 1/60000
	48	−	−	−	−	−	−	−	−	−	−	−	−	
	72	−	−	−	−	−	−	−	−	−	−	−	−	
Ortho-aminophenol ...	24	−	−	−	−	−	−	−	−	−	−	−	−	Upto 1/50000
	48	−	−	−	−	−	−	−	−	−	−	−	−	
	72	−	−	−	−	−	−	−	−	−	−	−	−	

− =Inhibition of growth. + =Growth. L.M. =Peptone media. S.M. =Taurocholate agar media.

TABLE 3—SUMMARY OF THE EFFECTS OF THE COMPOUNDS ON DIFFERENT BACTERIA

Name of the compound	Name of organism inhibited with dilution of compounds					
	Vibrio cholerae	Strep. haemolyticus	Esch. coli	Salmonella typhi	Shigella shigae	Staph. aureus
Thiocarbamide	—	Upto 1/1000	—	—	Upto 1/1000	Upto 1/2000
Benzylthiocarbamide	Upto 1/2000	Upto 1/4000	—	—	—	—
N'-N'-Dibenzylthiocarbamide ...	—	—	—	—	—	—
Orthothiocarbamidophenol ...	Upto 1/32000	Upto 1/16000	—	Upto 1/1000	Upto 1/2000	....
3'-3'-Dihydroxythiocarbamidophenol	Upto 1/8000	—	—	Upto 1/500	Upto 1/500	Upto 1/1000
4'-4'-Dihydroxythiocarbamidophenol	Upto 1/40000	Upto 1/2000	—	Upto 1/2000	Upto 1/16000	Upto 1/2000
Metathiocarbamidophenol ...	—	—	—	—	—	—
Paracarbamide	Upto 1/16000	Upto 1/1000	—	—	—	Upto 1/1000
Para-aminophenol	Upto 1/60000	Upto 1/16000	—	Upto 1/1000	Upto 1/2000	Upto 1/2000
Ortho-aminophenol	Upto 1/50000	Upto 1/16000	—	Upto 1/1000	Upto 1/2000	Upto 1/2000

— =No inhibition in any dilution. .... =Not observed.

then watched for any untoward symptoms. As no untoward effects were noticed, the doses of all of them were gradually increased to 500 mg. per kg. body weight, also without any ill-effect. The two other compounds, e.g., para-aminophenol and ortho-aminophenol were subjected to the same tests in the laboratory of Messrs. Albert David Ltd., Calcutta, and were also found to be of low toxicity.

CLINICAL TRIAL

The patients were divided into three groups. Group A were given the compound to be tested in 2 to 4 g. doses, every 4 hours. Group B were given oxytetracycline, 500 mg. 4-hourly. Group C were given sulphaguanidine tablets, 4 g. four-hourly. In all the groups standard treatments with transfusion etc., were carried out. The patients selected were all pulseless and toxic, except in group B. Previous to the administration of any drug, catheter specimen of the stools were collected. Subsequent samples, during and after the administration of the drugs, were collected at four-hourly intervals, for bacteriological examination. The results are shown in Table 4. The clinical trial was carried on for twenty hours only in each case as it was felt that any drug taking a longer time in producing beneficial effects might not be considered therapeutically important in the treatment of acute cholera. The control without any antibacterial drug was thought unnecessary as the trial in each case was conducted for only twenty hours which was too short a period to produce any significant bacteriological change by itself.

RESULTS AND DISCUSSIONS

Out of the ten new compounds investigated in this series, four, as noted above, manifested pronounced antibacterial activity against *V. cholerae*. In addition, they showed inhibitory actions against some other bacteria also. Thus *Streptococcus haemolyticus* was inhibited in dilutions upto 1 in 16,000 by orthothiocarbamidophenol, ortho-aminophenol and para-aminophenol, while 4'-4'-dihydroxythiocarbamidophenol inhibited its growth upto dilution of 1 in 2000. In the same order, *Shigella shigae* was inhibited in dilutions upto, 1 in 2000, 1 in 2000, 1 in 2000, and 1 in 16,000, respectively, *Solmonela typhi* in dilutions upto 1 in 1000, 1 in 1000, 1 in 1000, and 1 in 2000 respectively, while *Staphylococcus aureus* had no inhibition in any dilution, with the first, but was inhibited in dilutions upto 1 in 2000, 1 in 2000, and 1 in 2000, respectively, with other three compounds (Table 3). In this connection it may be mentioned that the 'crude thiodiamine' during the earlier investigation, was empirically given to two patients, one suffering from mastoiditis and another from furunculosis. Both responded well. Unfortunately, none of the compounds, discussed above, were clinically tried for strepto- or staphylococcal infections. None of these compounds had any action on *Esch. coli* in any dilution.

Results of clinical trial in cholera (*Table 4*)—Orthothiocarbamidophenol was tried in 34 patients with 14 deaths (41·17 per cent), 4'-4' dihydroxythiocarbamidophenol in 8 patients with 4 deaths (50 per cent), para-aminophenol in 14 patients with 4 deaths (28·57 per cent), ortho-aminophenol in 10 patients with 2 deaths (20 per cent), sulpha-

TABLE 4—SHOWING EFFECTS OF COMPOUNDS ON *V. cholerae* IN STOOL

Serial No.	Initials & Age		Before administration of the drug	4-hourly stool sample after administration of compound					Remarks
				1st	2nd	3rd	4th	5th	
			ORTHOTHIOCARBAMIDOPHENOL						
1.	J.M.	25	++++						E
2.	T.B.	32	++++	++	++	++	+	+	C
3.	J.N.	36	++++	+++	+++				E
4.	G.P.	25	++++	+++	+++	+++	+++	+++	E
5.	N.C.	25	++++	+++	+++	+++	++	++	C
6.	B.P.	50	++++	+++	+++	+++	+++	+++	E
7.	A.B.	55	++++	+++	+++	+++	++	++	C
8.	D.B.	23	++++	+++	+++	+++	++	++	C
9.	R.C.D.	55	++++	+++	+++	+++	+++	+++	E
10.	B.D.	35	++++	+++	+++	+++	++	++	C
11.	M.	31	++++	+++	+++	+++	++	++	C
12.	S.M.	22	+++	+++	++	++	++	++	C
13.	A.K.	35	+++	+++	+++	++	++	++	C
14.	M.S.	20	++++	+++	+++	+++	++	++	C
15.	D.P.	45	++	++	+	−	−	−	E
16.	N.M.	45	++++	+++	+++	+++	++	++	E
17.	J.G.	17	+++	++	−	−	−	−	C
18.	B.M.	48	−	−	−	−			E
19.	T.	35	−	−	−				E
20.	A.K.N.	27	−	−	−				E
21.	R.S.	32	−	−	−				E
22.	J.G.	30	−	−	−				E
23.	A.B.	20	+++	++	++	+	+	−	C
24.	D.M.	22	++++	+++	+++	++	++	++	C
25.	A.D.	40	+++	++	++	++	+	+	C
26.	K.S.	35	++++	+++	++	++	+	+	C
27.	K.D.	40	+++	+++	+++	++	++	++	C
28.	A.G.	50	+++	+++	+++	−	−	−	C
29.	D.D.	25	+++	+++	+++				E
30.	S.P.	20	+++	+++	++	++	++	+	C
31.	M.M.	34	+++	+++					E
32.	S.D.	36	+++	+++	+++	+++	+++	++	C
33.	M.D.	38	++++	+++	+++	++	++	++	C
34.	P.D.	40	++++	+++	++	++	++	+	C
			4'-4'-DIHYDROXYTHIOCARBAMIDOPHENOL						
1.	S.S.	20	+++	++	++	++	++	++	E
2.	M.A.	40	+++	++	++	++			E
3.	P.S.	41	++	++	++	+	+	+	C
4.	J.G.	20	++	++	++	++	++	+	C
5.	A.T.	44	++++	+++	+++	+++	++	++	C
6.	A.R.	20	+++	+++	+++				E
7.	B.M.	15	+++	+++	++	++	±	−	C
8.	A.G.	26	+++	+++	+++	+++	++	++	E

+ =Growth. − =No growth. E=Expired. C=Cured.

TABLE 4—*Contd.*

Serial No.	Initials & Age		Before administration of the drug	4-hourly stool sample after administration of compound					Remarks
				1st	2nd	3rd	4th	5th	
				PARA-AMINOPHENOL					
1.	T.M.	55	++	++	++	+	+	+	E
2.	S.C.	28	++++	++++	+++	++	++	+	C
3.	K.B.S.	35	+++	++	+	±	−	−	C
4.	P.P.	37	++	++	++	±	±	±	E
5.	D.D.	20	+++	+++	++	++	++	+	C
6.	S.L.	50	++++	+++	+++	++	+	+	C
7.	B.M.	30	++++	+++	+++	++	++	++	C
8.	A.G.	22	++++	+++	+++				E
9.	T.S.	26	++++	+++	+++	++	++	+	C
10.	A.K.	30	+++	++	++	++	+	+	C
11.	B.G.	35	++++	+++	++	++	+	±	C
12.	D.S.	42	+++	++	++	±	±	−	C
13.	S.M.	45	+++	+++	++				E
14.	G.J.	22	++++	+++	+++	++	++	+	C
				ORTHO-AMINOPHENOL					
1.	A.G.	20	+++	+++	+++	++	++	+	C
2.	B.G.	15	++++	+++	+++	++	+	+	C
3.	M.N.	26	++++	+++	+++	++	+	+	C
4.	S.S.	30	+++	++	++	+	+	+	C
5.	A.N.	40	+++	++	++	++	+	+	C
6.	R.G.	25	++++	+++	+++	++	++	+	C
7.	R.G.	20	+++	+++	++	++			E
8.	R.M.	20	+++	+++					E
9.	S.T.	25	+++	+++	++	++	+	+	C
10.	B.G.	20	++++	+++	+++	++	+	+	C
				SULPHAGUANIDINE					
1.	N.M.	32	++++	++	++	++	+	+	E
2.	B.M.	45	++++	+++	++	++	±	±	C
3.	S.N.	22	+++	++	++	++	+	+	C
4.	T.D.	20	+++	++	++	++	+	+	E
5.	N.K.	20	+++	++	++	++	+	−	C
6.	L.M.	26	+++	++	++	++	+	+	C
7.	D.N.	17	+++	++	++	+	+	+	C
8.	N.G.	18	+++	++	++	++			E
				OXYTETRACYCLINE					
1.	S.D.	30	++	++	++	++	++	++	C
2.	M.T.	40	++	++	+	−	−	−	C
3.	C.D.	45	+	+	−	−	−	−	C
4.	C.N.	30	++	++	+	−	−	−	C
5.	G.G.	35	+++	+++	++	++	+	+	C
6.	N.G.	19	++	++	++	+	+	−	C
7.	T.M.	46	++	++	+	−	−	−	C
8.	S.H.	26	++	++	+	−	−	−	C

+ =Growth. − =No growth. E=Expired. C=Cured.

guanidine in 8 patients with 3 deaths (37·5 per cent), and oxytetracycline in 8 patients with no death. It may, however, be mentioned that these death rates are not strictly comparable for the assessment of the values of the individual compounds used, because of the facts that the compounds had to be used in different phases of the epidemic, according to their availability and also there was divergence in the total number of patients in each group. So it appeared more important to investigate the anti-bacterial actions of these compounds, in patients, by making four-hourly cultural examinations of their stools during the course of administration of these drugs.

In heavy infection, para-aminophenol, sulphaguanidine, and ortho-aminophenol, generally showed reduction in the infection from the third sample of stool after the administration of the compound and this became more noticeable in the fifth sample (20 hours). In this respect, the former two compounds appeared to be more active than the latter. As regards oxytetracycline, it will be apparent from Table 4 that the patients receiving this drug were mostly suffering from comparatively milder infection. In heavy infection this drug did not show any superiority over the three above-mentioned compounds. In milder infection the result with oxytetracycline was appreciably good, the stools in several persons becoming vibrio-negative from the third sample. But this result could not be compared with other groups as none of them contained any patient with milder infection.

None of these compounds produced any ill-effect on the patients.

Summary

Earlier investigation with a crude extract, named thiodiamine, showing good antibacterial actions against *V. cholerae* and later elucidation of the structural formulae of the same product, prompted the present investigation of some of the allied compounds. Ten new compounds, generally of phenyl and diphenyl linkages were investigated for their antibacterial properties. Four of them, e.g., orthothiocarbamidophenol, 4′-4′-dihydroxythiocarbamidophenol, ortho-aminophenol, and para-aminophenol, were found to have marked antibacterial effects against *V. cholerae, in vitro*. They also showed antibacterial actions against *Streptococcus haemolyticus, Staphylococcus aureus, Shigella shigae* and *Salmonella typhi*, in varying degrees. They had no action against *Esch. coli*. They were also found to have very low toxicity when orally administered to rabbits for a short time. On clinical trial, in cholera their effects on death-rates were inconclusive for various reasons. In heavy infection, on four-hourly cultural examinations of stool, antibacterial effect of para-aminophenol was found to be practically equal to that of sulphaguanidine or oxytetracycline. Effect of ortho-aminophenol appeared to be a little less. In milder infection where only oxytetracycline and not others were tried, the former showed good antibacterial action against *V. cholerae* in stool. Discrepancy between the actions of 'Crude thiodiamine' and its synthetic preparation is discussed. These compounds, especially the aminophenols, are not recommended for wider use without further trial. The present investigation only indicates that further research in the same line may yield valuable results in the long run.

Acknowledgments

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PRELIMINARY REPORT ON HYPOTENSIVE EFFECT OF RESERPINE

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Crude extracts of roots of *Rauwolfia serpentina* have been widely used in India in various ailments including agitated states and various forms of insanity. It was used as a hypotensive and sedative agent early in this century. The first report about its use in insanity and high blood pressure came from Sen and Bose (1931). Ray (1931) in the same year confirmed its sedative

action. Siddiqui and Siddiqui (1931, 1932) isolated many of the alkaloids from the roots of *Rauwolfia serpentina* in the early thirties. The study of pharmacology of extract of *Rauwolfia serpentina* was undertaken by Chopra *et al* (1933) and recently by Roy *et al* (1953) and Dasgupta *et al* (1953). Chopra *et al* (*loc. cit.*) reported that the alkaloids concerned were strong hypotensive agents. He ascribed the hypotensive effect to depression of the central nervous system and partly to inhibition of the musculature of the blood vessels.

Following these publications extensive clinical trials with extract of whole root of *Rauwolfia serpentina* followed throughout the world. The reports which appeared were conflicting specially with regard to the incidence of satisfactory response and appearance of toxic symptoms.

Muller *et al* (1952) isolated a new alkaloid reserpine from the oleoresin fraction of the crude rauwolfia. This oleoresin fraction was known to have the sedative action of the whole root. Pharmacological studies of this alkaloid have been published by Bein *et al* (1953a and 1953b) and Trapold *et al* (1954). They reported that the hypotensive action was effected through the central nervous system. It also has the capacity to inhibit reflex pressor responses.

A recent publication by Mc-Queen *et al* (1953) shows a comparative study of effects of large doses of reserpine in hypertensive and normotensive patients. Hypertensives show larger fall of blood pressure.

The initial experiments carried out with reserpine on the aggressive Rhesus monkey proved that the site of action of reserpine is the hypothalamus. In E.E.G. tracings, reserpine produces waves of low amplitude and high frequency unlike barbiturates which produce waves of high amplitude and low frequency, resembling a 'sleeping pattern' of E.E.G. Thus reserpine, while exerting a marked tranquillising action on the hypothalamus, the centre for emotional behaviour, does not produce narcosis typical of barbiturates. This 'awaking pattern' of E.E.G. permits high doses of reserpine to be administered without the untoward effects seen with barbiturates.

Almost simultaneously with the study of pharmacological effects of this new crystalline pure alkaloid from *Rauwolfia serpentina* a number of clinical reports appeared. Loffler *et al* (1953) found some hypotensive effect in 28 per cent of his cases. Vakil (1940) noted a fall of both systolic and diastolic pressure in 72 per cent with minimal side reactions.

Doyle and Smirk (1954) produced a considerable fall of both systolic and diastolic pressure in 6 out of his 9 patients with single doses of 2 or 3 mg. of reserpine by mouth. The response was obtained in a few hours' time.

Results of Douthwaite (1954) with oral reserpine in varying doses were significant. 10 out of 12 cases had significant fall of blood pressure.

In a recent article, Inder Singh (1955) concludes that reserpine is a useful drug in the treatment of all types of hypertension. It lowers the blood pressure to normal or to within reasonable limits in all cases of less chronic and less severe benign hypertension, and the same effect may also be obtained in some of the more chronic and severe cases.

Doyle *et al* (1955) using small doses of reserpine, so as not to produce side effects, treated 40 patients with hypertension. Therapeutically useful fall of blood pressure was obtained in 10 cases only.

A clinical trial with reserpine orally in arterial hypertension was carried out in the department of cardiology, R. G. Kar Medical College & Hospitals, Calcutta to find out :

(i) The incidence of lowering of B.P. and quanta of fall amongst a large group of patients ; (ii) the time required to attain maximum fall of B.P. ; (iii) myocardial changes, if any, during reserpine therapy ; (iv) the incidence and nature of side effects and (v) the types of cases refractory to reserpine therapy.

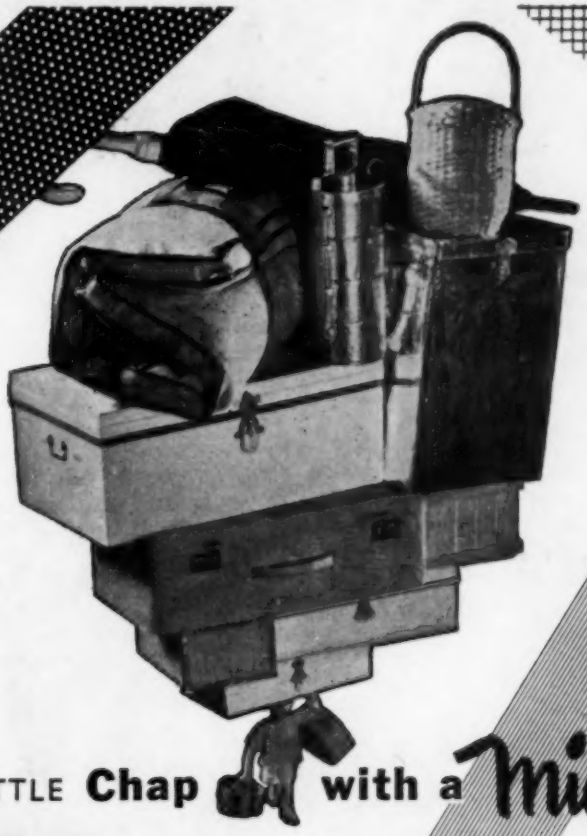
Method and Materials

A total of 60 ambulant patients attending the out-patients' department in course of one year were selected for study. We were careful to select those cases whose blood pressure, particularly diastolic pressure, did not show wide fluctuations, and who had not been treated before. Some fluctuation in basal B.P. was observed and we recorded the lowest level as the basal one.

(2) Blood pressures were recorded bi-weekly by one individual in the same room in the recumbent posture.

(3) Ordinarily a basal diastolic pressure of 100 mm. of Hg or over, was considered suitable for trial. We have included a few exceptional cases who had hypertension previously and had other stigmata of hypertension, i.e., enlarged heart, ringing aortic second sound, but had a diastolic pressure up to 90 mm. of Hg during the course of trial.

(4) All cases were thoroughly examined clinically and fluoroscopically before treatment. All had E.C.G. done before therapy, and repeated sometime after the maximal fall had been obtained. QTC's were determined. Routine urine analysis was done in every case.



The LITTLE Chap with a Mighty lot...

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TABLE 1—SHOWING THE EFFECTS OF RESERPINE

Serial No., Name, Age & Sex	Clinical state before therapy	Blood Pressure S/D			Duration to attain maximum change of B.P.	Clinical state after maximum change	E.C.G. changes
		Basal	Maximum change	% of fall			
1. C.D., 47 M	L.V. failure. Auricular fibrillation	150	125	20	7 days	Dyspnoea increased for which digitalis & mercurial diuretics were given	Nil
		100	85	15			
2. N.B.S., 66 M	Vertigo	170	145	14	4 months	Vertigo persisted	Nil
		105	85	19			
3. J.B., 59 M	Exertional dyspnoea	158	150	5	2 days	Dyspnoea continued. Relieved by digitalis	Nil
		110	100	9			
4. B.B.A., 50 M	Emphysema, bronchial asthma	160	160	...	3 weeks	No response	Nil
		110	120				
5. B.K.D., 61 M		170	150	12	2 days	Satisfactory	Nil
		100	90	10			
6. R.D., 72 F	Bronchial asthma	160	165	...	8 weeks	No response	Nil
		100	100				
7. J.B.D., 46 M	Auricular fibrillation. Cardiac failure	140	130	7	4 weeks	Digitalis supplemented	Nil
		105	90	14			
8. N.C.D., 51 M		154	130	15	4 weeks	Satisfactory	Nil
		105	90	7			
9. G.B.C., 50 F		250	150	40	4 weeks	Satisfactory	Sinus bradycardia (54 per minute). High 'T' waves
		120	70	40			
10. L.P., 25 F	L.V. strain, myocardial ischaemia	170	165	3	4 days	Giddiness	Nil
		125	120	3			
11. K.L.M., 65 M		180	220	...	5 weeks	No response	Nil
		105	110				
12. P.K., 35 F		170	125	26	4 days	Satisfactory	Sinus bradycardia. High T waves, appearance of "U" waves
		120	85	29			
13. N.M., 65 F		180	145	19	8 weeks	Satisfactory	Sinus bradycardia
		110	90	19			
14. R.C.B., 53 M	Subacute stage. Post infarction. Mild L.V. failure	165	145	12	6 weeks	Died suddenly of pulmonary oedema while not on reserpine therapy	?
		90	80	15			
15. L.C.B., 62 M	Cardiac enlargement, apical systolic murmur, left B.B. block	220	170	22	2 weeks	Satisfactory	Sinus bradycardia
		130	80	39			
16. L.B.R., 49 M		220	155	29	4½ weeks	Satisfactory	Marked sinus bradycardia. High T waves
		135	90	39			
17. K.C.B., 55 M	L.V. strain, myocardial ischaemia	190	130	32	3 weeks	Giddiness, diarrhoea	Nil
		110	70	36			
18. M.L.M., 81 M	Cardiac enlargement. Left B.B. block	220	190	13	10 weeks	Giddness	Nil
		100	80	20			
19. N.C.D., 39 M	L.V. strain, cardiac failure	230	175	24	9 weeks	Digitalis supplemented. Good response	Nil
		150	100	33			
20. N.K.S., 23 F		190	130	36	10 weeks	Satisfactory	Sinus bradycardia
		135	85	37			

TABLE 1—*Contd.*

Serial No., Name, Age & Sex	Clinical state before therapy	Blood Pressure S/D			Duration to attain maximum change of B.P.	Clinical state after maximum change	E.C.G. changes
		Basal	Maximum change	% of fall			
21. N.D.D., 60 M	Prolonged P-R. Cardiac enlargement	200	170	15	9 weeks	Mild giddiness	No further prolongation of P-R
		100	95	6			
22. M.D., 54 M	L.V. hypertrophy and diabetes mellitus	180	155	14	7 weeks	Marked giddiness	Nil
		90	70	22			
23. A.B.P., 62 M	L.V. hypertrophy and strain	200	150	24	8 weeks	Satisfactory	Sinus bradycardia
		110	55	21			
24. N.H., 65 M	L.V. hypertrophy	250	160	32	4 weeks	Satisfactory	Nil
		145	90	37			
25. A.C.A., 43 M		150	120	20	4 weeks	Good	Nil
		95	80	15			
26. C.M.G., 63 M	Rt. B.B. block	170	160	6	8 weeks	Fair	No further increase of intraventricular conduction defect
		110	90	18			
27. B.B.R.. 57 M		200	160	20	3 weeks	Satisfactory	
		105	85	18			
28. J.C.R., 50 M		180	140	21	4 weeks	Fair	Sinus bradycardia
		110	95	13			
29. G.C.S., 62 M		150	135	10	2 weeks	Fair	Sinus bradycardia. High T waves
		100	85	15			
30. J.S., 42 M	L.V. strain.	220	160	27	10 days	Satisfactory	Sinus bradycardia
		110	80	27			
31. H.M.R.,62 M	L.V. hypertrophy	180	130	28	2 weeks	Good	Nil
		90	75	16			
32. D.K., 44 M		170	130	23	7 days	Good	Nil
		105	80	24			
33. N.S., 62 M	Rt. B.B. block. Severe diabetes mellitus	220	180	18	4 days	Fair	No change in intraventricular conduction
		130	95	27			
34. B.K.D., 59 M		190	150	21	3 days	Good	Nil
		120	90	25			
35. S.K.B., 61 M	L.V. hypertrophy. Rt. auricular enlargement, chronic bronchitis with emphysema	195	200	...	4 weeks	No response. Developed oedema feet & face disappearing on discontinuing the therapy	Nil
		130	140				
36. B.A., 60 M	L.V. hypertrophy, myocardiac ischaemia. S.T. depressed in standard leads.	210	165	21	10 days	Fair	Persisted
		110	85	22			
37. T.N. 65 M		200	125	37	7 days	Good	Nil
		130	85	44			
38. J.G., 35 F		155	175	...	4 weeks	No response. Marked bradycardia. Oedema feet	Nil
		100	100				
39. B.S., 68 M		175	125	28	6 days	Bradycardia and nasal congestion. Giddiness	Nil
		110	65	32			
40. M.N.S., 60 M		180	130	27	18 days	Bradycardia	Nil
		105	75	27			

TABLE 1—*Contd.*

Serial No., Name, Age & Sex	Clinical state before therapy	Blood Pressure S/D			Duration to attain maximum change of B.P.	Clinical state after maximum change	E.C.G. changes
		Basal	Maximum change	% of fall			
41. R.K., 40 M		160	115	28	12 days	Bradycardia	Nil
		100	70	30			
42. H.M.D., 35 F	Cardiac enlargement. Apical systolic murmur	180	140	22	4 days	Bradycardia	Nil
		130	85	34			
43. S.K.M., 52 M	Chronic cor pulmonale	180	170	...	4 weeks	Oedema legs disappeared on stoppage of therapy	Nil
		120	130				
44. P.K.C., 32 M		230	170	26	3 weeks	Marked giddiness	Nil
		120	110	8			
45. P.D., 47 F	L.V. failure. Cardiac asthma	160	150	6	3 weeks	Simultaneously digitalis & mercurial diuretic were given	Nil
		100	80	20			
46. M.L.B., 52 M		210	160	24	3 weeks	Good	Nil
		100	80	20			
47. S.D., 26 F		185	170	9	17 days	Fair	
		130	100	23			
48. R.K.M., 30 M		150	110	27	3 days	Satisfactory	Sinus bradycardia
		100	70	30			
49. K.C.G., 65 M		190	200	...	50 days	No response, giddiness, nasal congestion. Oedema legs & puffiness of eyelids	Nil
		95	95				
50. P.K., 46 M		170	150	11	2 weeks	Fair	Sinus bradycardia
		110	90	18			
51. M.A., 50 M	Chronic bronchitis with emphysema. Rt. B.B. block	220	210	...	4 weeks	No response	Nil
		130	150				
52. S.R.S., 31 F		135	130	4	4 days	Fair	Nil
		95	80	15			
53. K.B.D., 34 F		170	130	24	4 days	Good	Nil
		110	80	27			
54. I.P.G., 35 F		155	175	13	25 days	Marked giddiness. Bradycardia. Nodal rhythm	Nil
		110	80	18			
55. S.K.M., 60 M	Prolonged P.R. interval. Premature beats. L.V. failure	170	130	29	6 days	Good	Nil
		120	80	33			
56. N.L.L., 65 M		180	180	...	11 days	No response. Giddiness & severe mental depression	Nil
		120	120				
57. B.C.B., 64 M		210	210	...	10 days	No response, diarrhoea and giddiness	Nil
		100	100				
58. R.K.S., 59 M		210	190	9	6 weeks	No symptomatic relief	Nil
		110	100	9			
59. J.C.S., 41 M		220	200	9	15 days	No relief. Haematuria and epistaxis	Nil
		165	150	9			
60. M.L., 42 M		180	140	22	3 weeks	Oedema of feet and puffiness of face after 4 weeks	Nil
		120	100	16			

The dose of reserpine was small and varied from 0·3 mg. to 0·75 mg. daily according to the severity of basal blood pressure. The results are shown in Table 1. Only certain special signs and symptoms and complications before therapy are noted under the heading 'clinical state'. Those who showed only manifestations of anxiety neurosis are left blanks.

Thirty per cent of the patients required two weeks or less to attain maximum fall of diastolic pressure and majority attained maximum hypotensive effect in course of 4 weeks. 8 per cent of cases took more than 6 weeks when the maximum fall was attained.

Amongst the 9 cases who did not register any fall of pressure, 5 were subjects of emphysematous bronchitis.

Electrocardiographic changes—Roy Chowdhury and Ghosh (1953) reported E.C.G. changes with a particular microcrystalline fraction of Rauwolfia. They noted sagging RST segment over L.V. surface as well as some lowering of T waves in some of their cases.

On close scrutiny of every E.C.G. we found no gross changes solely due to reserpine. Bradycardia was of sinus origin. 4 cases presented very high T waves (10 mm.) over R.V. surface. No further prolongation of intraventricular conduction was noted with long continued reserpine therapy in cases presenting gross intraventricular conduction defect before the trial. R.-S.-T deviation was not significant.

No gross T wave changes were noted. Corrected QT values did not show any deviation from the previous one as determined before reserpine therapy.

Side-effects—The incidence and nature of side-effects are shown in Table 2.

That the side-effects were due to reserpine could be proved by the fact that all of them disappeared in a week's time after temporary discontinuation of the drug.

TABLE 2—SHOWING INCIDENCE AND NATURE OF SIDE-EFFECTS

	No. of patients	Percentage
Severe depression and lethargy ...	3	5
Mild to severe giddiness ...	11	18
Nasal stuffiness	4	6
Puffiness of face and oedema of eyelids	3	5
Bradycardia (heart rate less than 60 per minute)	15	25
Nodal rhythm	1	—
Diarrhoea	2	—

An interesting side effect was noted in 3 patients during reserpine regime in the form of facial oedema and puffiness of eyelids. The symptoms disappeared in one week's time after stoppage of the drug. Mechanism of such oedema could not be explained. Reserpine may have an antidiuretic effect through the pituitary as has been shown in animals by Gaunt *et al* (1954).

SUMMARY

(1) Seventy per cent of this series showed hypotensive effect with small dose of reserpine when given orally.

(2) Majority of them attained maximum fall of diastolic pressure within 4 weeks. Delayed response, i.e., more than 6 weeks was obtained in 8 per cent.

(3) Serious side effects were not noted with the doses employed.

(4) Out of 10 patients who did not register any fall of pressure, 5 were emphysematous subjects with chronic bronchitis.

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PRACTITIONERS' SERIES

NUTRITIONAL OEDEMA SYNDROME IN CHILDREN

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Nutritional oedema syndrome is commonly met with in pediatric practice. This disease is seen in children of all ages and may be produced by dietetic insufficiency or may be a secondary result of some other primary disease which increases the nutritional needs of children or decreases their appetite or interferes with the process of digestion and absorption of food in the alimentary canal. Chronic respiratory tract diseases, chronic diarrhoea and tuberculosis produce malnutrition in children. Under-nutrition is not in protein deficiency alone but is usually accompanied by other specific mineral and vitamin deficiencies. This syndrome is commonly seen in children of the poor classes. In older children the state of under-nutrition may be either a continuation of the same state from infancy or due to chronic infections, mostly of the gastro-intestinal and respiratory tracts.

The principal causes of this syndrome are poor diet (consisting mainly of carbohydrates and very little of proteins, particularly milk) and chronic gastro-intestinal infections.

Eighty one cases of nutritional oedema syndrome were seen at Sir Takhtasinhji Hospital, from January 1952 to October 1955. There were 56 male and 25 female children. Of these, 60 came from poor social status, 14 from middle class and 7 from upper middle class families. The age group is shown in Table 1.

TABLE 1—SHOWING AGE INCIDENCE

Age groups	No. of cases
0— 6 months	1
7—11 months	4
1— 3 years	28
4— 5 years	21
6—10 years	27

Diet—The diet of poor class children consisted mainly of cereals (*jowar, bajri* and occasionally wheat) and butter milk with milk added only rarely and no fruits. The diet of middle class children consisted of cereals (wheat and *bajri*), *dal*, rice, vegetables and daily intake of milk (only little quantities) and no fruits. History of breast feeding was obtained in 90 per cent of the children which was continued till 1½—2 years of age.

CLINICAL FEATURES

Oedema—The onset of oedema was sudden in 23 cases and gradual in the rest. It was slight in 24 cases, moderate in 46 and severe in 11 cases. The common sites of oedema were feet, legs and face. Anasarca was seen in 4 cases. Ascites was present in 17 cases. All, except one, were admitted into the hospital with oedema as one of the complaints. This single case developed oedema after admission for the treatment of chronic diarrhoea. The oedema was of fluctuating type (appearing and disappearing) in 7 cases.

Retarded growth—It was observed in 66 cases.

Skin and hair changes—The skin was dry in 30 cases. In 3 cases superficial layers of the skin were seen peeling off in small whitish scales. Boils and ulcers all over the skin were observed in 2 cases. Maceration of the skin with cracks and fissures round the anus was found in 3 cases. Crazy pavement pigmentation was present in 15 cases and pellagrous type of pigmentation in 45 cases. Phrynoderma was seen in 15 cases and follicular hyperkeratosis in 2 cases. Stumps of broken hairs were seen in 7 cases. Light coloured hairs were seen in 32 cases.

Vitamin deficiency—The incidence of various forms of vitamin deficiency are shown in Table 2.

TABLE 2—SHOWING VITAMIN DEFICIENCIES

Specific deficiencies	No. of cases
Xerosis	22
Bitot's spots	9
Hazy cornea	1
Corneal ulcer	1
Angular stomatitis	10
Glossitis	8
Stomatitis	12
Bleeding hypotrophied gums ...	3

Mental apathy—It was noticed in 82 per cent and irritability in 5 per cent of cases.

Anaemia—It was a feature in 70 cases (mild 17, moderate 40 and severe 13). Anaemia was pre-

dominantly microcytic and only in 5 cases it was macrocytic in type.

Liver and spleen—The liver was enlarged in 32 cases. It was soft in feel in all the cases. The spleen was enlarged in 9 cases.

Respiratory system—Upper respiratory tract infection was present in 44 cases. Four cases had primary complicated tuberculosis of the lungs, one of whom expired due to tuberculous bronchopneumonia.

Cervical adenitis—Slight to moderate enlargement of the cervical lymph glands was seen in 20 cases.

Urinary system—Oliguria was noticed in 5 cases. These patients were not dehydrated. The mothers of these children also complained that they passed scanty urine. These cases had no other abnormality in the urinary system. Urine examination showed presence of albumin in 17 cases. Urine was otherwise normal. Blood urea in these cases were within normal limits.

Stools—Frequency of stools in its acute or chronic form or its past occurrence before the onset of oedema (just before or sometime before) has a very important aetiological significance in the nutritional oedema syndrome. Past history of dysentery or diarrhoea (a few days to a few months ago) was available in 8 cases. 26 cases had chronic diarrhoea and 16 cases had chronic dysentery at the time of admission. 5 cases were admitted for acute dysentery. Incidence of amoebic infection was very low in these children (only 3 cases). Most of these cases had pus and mucus in stools and thus it is presumed that they were cases of either chronic bacillary dysentery or chronic infective diarrhoea. Ascariasis was found in only 2 cases. No case of steatorrhoea was seen.

Summary

81 cases of malnutrition, admitted into a hospital in Saurashtra from January 1952 to October 1955 are described. The maximum incidence was noted in the age period between 1 and 3 years. The syndrome was seen in more than 75 per cent in poor classes. The features consisted of oedema, retarded growth, changes in the skin and hair, mental apathy, anaemia, hepatomegaly and specific deficiencies of vitamins A and B complex.

In children of higher age groups a peculiar yellowish brown muddy coloured band was noticed running across the eye extending from both canthuses of the eye upto sclerocorneal junctions. The band appeared to be slightly elevated from the surface of the conjunctiva.

SPECIAL ARTICLE

MEDICAL STUDENTS, MEDICAL LITERATURE AND LIBRARIES

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Books, journals, pamphlets, etc., as records of man's experience and achievements, are indispensable to progress, especially in a field as specialised and as technical as medicine. Libraries, as institutions collecting these records and disseminating knowledge, have come to be regarded as one of the most necessary constituents in the group of agencies essential to the furtherance of medical education, research, and therefore, medical relief. It is not surprising that among the papers read and discussed at the First World Conference on Medical Education was one on Library and Reference Service (Rogers, 1953). In our country the McDonald Report of 1945, the Bhore Committee Report of 1946 and the Medical Education Committee of the Madras Medical and Public Health Conference of 1947, emphasised the need for well equipped and well managed libraries in every medical institution to aid the student in his studies, the teacher in his teaching, the research worker in his researches, and to provide the general practitioner with the latest and correct information in the field.

To the medical student a knowledge of and familiarity with library services and the various aids for exploring the literature of the medical sciences would be a great asset though it may not be immediately apparent to him at the undergraduate level. The British Medical Association Medical Curriculum Commitee in its Report (1948), while warning against too much dependence on textbooks, recommended systematic use of the library by the student. The committee recommended the following:

"Beginning in his first year and reinforced by later precepts, the student should be made aware of the great stimulus to knowledge afforded by independent reading, and the importance of supplementing by his reading both systematic lectures and practical work in laboratory and clinic. He must be able to use standard textbooks and periodicals intelligently and he should be directed to original papers which will satisfy his curiosity and, in the best student, incite the zest for research. . . . The library is indispensable and the student must be guided in its use, so that in his later professional life he will have in it a constant ally and friend."

It has been complained that

"At present far too many scientists graduate without ever having thoroughly learnt where and how they can

most probably expect to find information on any particular subject. To track down information speedily and successfully requires both a wide general knowledge of the bibliography of science and a knowledge of modern library practice." (*Endeavour*, 1950).

Further, regular and intelligent use of the library and literature would help to create in the student, library and book consciousness, provide him with a wider background to his studies, make him aware of the inter-relationship between the various disciplines, and the evolution, precepts and philosophies of his profession, all of which go to make him a better medical man.

When the student becomes a teacher or research worker his need to be familiar and thorough with all that goes on in his and related fields, cannot be overestimated. In the progress of research the library is a vital link for

"The first task of a scientist entering a field of research is to master the facts already discovered by earlier workers and then to keep abreast of the discoveries of his contemporaries pursuing the same line. In theory, this process is very simple; in practice, the barriers between the research worker and the facts he needs are often so formidable as seriously to impede the progress of science. In many fields, the accumulation of earlier work and the output of new publications are so great that research in the laboratory is outweighed by that in the library." (*Endeavour, loc. cit*).

It may be true that the research worker busy with his experiments has little time to spend in literature search and that he is not as well acquainted as the librarian with bibliographic techniques and literature search procedures, but it is well to remember that the research worker is the one who knows best his subject, its ramifications and collateral interests, and hence the librarian's approach to the problem will not be in the same line as that of the scientist. The orientation in the subject which the worker gains in searching the literature is quite so important to the project itself. Secondly, search and collection of the literature should be considered as an integral part of the research project and not as something apart from it; third, few libraries can afford a full scale and extensive bibliographic service needed by research and the scientist will have to depend to a great extent on his own abilities to explore the literature of the topic using available library facilities. While some schools may require term papers needing library use and literary effort, in a good graduate medical fellowship programme "the library, informal and formal conferences, seminars, staff and medical society meetings, case reports and scientific papers all serve educational objectives" (Allen, 1946). Obviously all these programmes and projects call for systematic use of the library. Thus, at all stages of medical education knowledge of the use of the library and methods of literature search is a great advantage to the medical student.

Three quarters of a century ago Billings, the founder of the Index-Catalogue, addressing the International Congress of Medicine in 1881 remarked that for the research worker ". . . a knowledge of how and where to find the record of a fact is often of more practical use than a knowledge of the fact itself". That was a time when library techniques and medical bibliographies were just developing in some parts of the globe. In the course of the century there have been created quite a number and variety of reference tools to the literature of the medical and allied sciences so that the medical man of to-day is not so much concerned with the creation of indexes to medical literature than with the learning of the intelligent use of the great number of reference works already available.

If any familiarity with library practices and medical reference works is to be developed in the medical man for his own benefit he must be taught young. Such 'Library Instruction' should become part of the undergraduate's curriculum. In the United States, the United Kingdom and some of the continental countries such programmes are becoming pretty well established. "In the United States more than half the schools give instruction in the use of the library and in bibliographic method" (Rogers, 1953). Our medical colleges too should plan such programmes of library instruction. The college authorities, the faculties as well as the library should cooperate in chalking out a course which while it does not interfere with the regular medical course is made compulsory, continuous, and of such duration that all necessary points of instruction are covered complete with practical work and assignments. If the departments would also make assignments needing library use it would be doubly beneficial to the student, for while he learns the use of the library it would be of immediate practical value to him.

The librarian and his assistants would normally be the most suitable persons to conduct such classes. This, of course, presupposes that the librarian is well qualified and fully competent for the job. He should have faculty status and teaching responsibilities. He should be planning ways and means of making the otherwise drab instructions interesting and create a zest in the listeners for the use of the records of human experiences. He has at his disposal all the modern audiovisual techniques of instruction to make his illustrations graphic and impressive.

For the post-graduates and those undertaking research (who would have had some experience

in library use) the specialty departments in association with the library could usefully organise seminars to discuss the progress of the literature in the specialty, the principal contributors and their contributions, related interests, special problems of literature search, the various special and general reference tools available in the field. Advice regarding note taking, thesis writing, obtaining material on interlibrary loans, as photocopies, and related questions, would be appreciated by them.

It may not be out of place at this point to briefly outline the syllabus for a library instruction course, and to those interested it would give some idea of things to be learnt.

The Library

General plan of the library—The location of stack room, reference works, bound volumes of periodicals, current back issues of periodicals, display of latest issues of journals, pamphlets and reports, display of new books. A plan of the library with the above locations marked may be given to students as a sort of a brochure containing other details about library and library rules.

General and special services offered—Membership and borrowal facilities to various categories of readers. Special collections, e.g., student textbooks, for nurses, for pharmacy students, etc., if any. Translation service, interlibrary loan and borrowal facilities, microfilm reading equipment, etc.

Circulation procedures and rules related thereto.

Aids in the use of the library—The various guides in the stack room ; brief explanation of the classification system and arrangement on the shelves of books and periodicals.

The library catalogue : What it is and how best to use it ; explanation of the various types of entries, the variety of information given on the cards ; location of items through author, subject, title or other approach ; symbols used to indicate items in different locations, e.g., departmental libraries, reference collection, rare book and locked sections. Use of the catalogue for various purposes.

Records of periodical holdings : catalogue, visible index system or any other method used.

Record of other serials : annual reports, etc. Record of pamphlets and reprints.

Reference Works in the Medical Sciences

Dictionaries—Their use besides finding the meaning, e.g., brief biographical information, illustrations, tests, etc. The chief medical dictionaries and their special points. Some of the foreign language medical dictionaries.

Encyclopaedias, compendiums, handbooks—Their value in obtaining basic, authoritative information, and lead to other literature sources. The important looseleaf systems.

Directories—They are for biographical data, addresses, information regarding societies and associations, their work and publications. Other miscellaneous information that may be found, in particular directories.

Medical periodical literature—Brief introduction on the growth of scientific societies and their transactions. The coming of the journals (general scientific) and later for each branch of knowledge and for various specialties. The vastness of medical literature published in journals and the need for indexing and abstracting services. The types of indexing and abstracting services :

Reviewing type : Annuals, 'recent advances', 'advances in' and similar series, review journals, review sections in journals.

Indexing and abstracting services : Indexes including closed ones, abstracting services, special bibliographies, current literature and abstracting sections in journals.

Other Useful Information

Bibliographic citation : forms and parts ; the common abbreviations used in medical literature citations.

Noting down references, form and fullness.

Need for exact statement of specific subject of search.

For the post-graduates information about some of the Union catalogues for location of periodicals in various libraries, facilities for inter-library loans and rules related thereto, obtaining material as photoreproductions from various sources.

Practical Work

This comprises of : Assignments in location of items in the library ; Use of the library catalogue ; Bibliographic citations ; Use of indexes and abstracting tools.

After the general lectures, the students should be divided into batches of convenient size and taken around the library indicating things explained, demonstrating use of the library catalogue, and then use of the reference works particularly the chief indexing and abstracting works.

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CASE NOTES

MIKULICZ'S DISEASE

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Mikulicz's disease is a rare entity with an unknown aetiology. Till recently, various names have been given to this disease and had to be differentiated from a group of diseases known as Mikulicz's syndrome. It was in 1888 Johann Mikulicz described this disease in a 42-year old man who came in for bilateral, chronic, painless hypertrophy of the lacrimal and salivary glands. He was of the opinion that this condition was one of chronic, low grade infection. Napp (1907) declared this condition to be merely a symptom complex that might be produced by any one of the several causes such as leukaemia, malignant lymphoma, tuberculosis, etc. Howard (1909) reviewed 81 cases collected from the literature and grouped them under three headings : Mikulicz's disease proper, malignant lymphoma and leukaemia. Swinton and Warren (1938) added seven more cases to the literature. Skorpil (1942) recorded a benign lymphoma of salivary gland and added 11 more cases to the literature. Morgan and Castleman (1953) reviewed 18 cases and gave an exhaustive clinicopathological study of the disease and are of the opinion that this disease is a definite entity by itself. Biopsy and autopsy review of the pathology department, Andhra Medical College as well as the statistics of King George Hospital did not reveal a single case of Mikulicz's disease and we have come across the following case first time in these parts. The case is reported for its rarity and to show the dramatic recovery with deep x-ray therapy treatment.

CASE REPORT

T. S., a Hindu male, aged 50 years, was admitted on 24-6-1955 for swelling of both the eyelids and parotid regions for ten months. The swelling started first on the right upper lid and the lateral extremity of the eye and began to increase in size gradually. Four months later, the patient noticed a swelling of the parotid and submandibular regions on the same side. This was followed two weeks later by swelling of the other eyelid and the parotid gland.

Examination of the patient (Figs. 1 and 2, *vide* Plate) revealed a diffuse, uniform swelling over the areas mentioned. Skin was freely movable over the swelling with no pain or tenderness. The masses of the right and left eyelids were hard, fleshy, projecting from the inner aspect. Swelling over the parotid region was irregular and not tender and did not show any sign of inflammation. Submandibular and submental glands were palpable. A few of them were discrete and a few matted. No other glands were palpable elsewhere. Other systems : nothing contributory.

Investigations—X-ray of the skull and chest—nothing significant. Urine and stools—no abnormality. Schimmer's test—negative. Mantoux test —negative. W.B.C.—6,250/c.mm. with polymorphs 58 per cent, lymphocyte 20 per cent, eosinophils 18 per cent, monocytes 2 per cent, basophils 2 per cent. R.B.C.—4·12 mill/c.mm. W.R.—negative. Total serum proteins—6 g. per 100 c.c.

Tissues from the lacrimal, parotid and submandibular glands were taken for biopsy examination. The lymph node showed moderate enlargement and uniform surface. Cut section was homogeneous in appearance. There was general overrunning of the architecture and replacement by a uniform, round cell pattern. Only traces of follicular structure were identified.

Lacrimal gland showed loss of complete architecture with replacement by uniform round cells. Some of them were mature. Few hyalinised islands could be made out ; no lymphofollicular pattern could be seen.

The parotid gland also revealed a similar loss of architecture, leaving behind no trace of the normal gland. The gland was completely occupied by both mature and immature lymphocytes. Some of the cells were in actual mitosis. There were islands of hyalinised lesions with peripheral flattened cell, showing the typical appearance of myo-epithelial island characteristic of a late stage of the disease (Fig. 3, *vide* Plate) A few of such islands could be seen. Some of them were in varying degrees of hyalinisation. The periglandular fat was infiltrated with the uniform round cells.

Diagnosis—Mikulicz's disease.

TREATMENT

Sulphadiazine, penicillin, liver extract, vitamin B complex were administered. He was also

treated with deep x-ray therapy with 16 exposures, 8 on each side. Strength of each exposure was 200 kilowatts/apm. After the course of deep x-ray therapy, swellings completely disappeared. Unfortunately, we could not get a photograph of the patient after treatment as the patient left the hospital without informing us.

SUMMARY

A case of Mikulicz's disease with complete recovery after deep x-ray therapy is recorded.

ACKNOWLEDGMENTS

We are very grateful to Dr. S. Venkateswarlu, Radiologist, King George Hospital, for the help rendered. We are also thankful to Dr. D. Govinda Reddy, M.D., Professor of Pathology, for his valuable guidance in preparing this paper. With pleasure we acknowledge the help rendered by photo-artist, A. S. Edwin.

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HAEMORRHAGIC COMPLICATIONS OF DUODENAL DIVERTICULA

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Duodenal diverticula are rarely encountered during routine barium meal examination of the gastro-intestinal tract. The pathological anatomy of duodenal diverticula has been exhaustively discussed in textbooks of radiological diagnosis. Whitmore (1948), in his excellent article, has discussed the symptomatology and complications. The diverticula may be symptom-free or might produce vague upper abdominal pain and discomfort of a chronic nature. If a diverticulum is large enough and there is stasis in it, it might produce pressure on the bile duct or pancreatic duct or might undergo inflammatory changes involving the pancreas—leading to symptoms of chronic cholecystitis, chronic pancreatitis, chronic peptic ulcer or even incipient carcinoma.

Complications which might arise from duodenal diverticula are ulceration, haemorrhage, perforation and, on rare occasions, calculus formation or adenocarcinomatous changes.

The two cases, reported below, came to the hospital with profuse haematemesis and melaena.

CASE REPORTS

Case 1—K. P. S., Hindu male, aged 70 years, was admitted on 16-5-54 with history of melaena (twice) and haematemesis (once) since 15-5-54.

Past history of epigastric pain relieved by food, for the last 30 years, with periods of remissions and exacerbations and for which the patient lived on bland diet during the above-mentioned period. At the time of admission, his blood pressure was 110/65 mm. of Hg. Pulse was 78 per minute and respiration, 20 per minute.

Laboratory investigations: Hb.—65 per cent, R.B.C.—3·2 million/c.mm., W.B.C.—7800/c.mm.

Blood urea—8·6 mg./100 c.c.,

Urine showed no abnormality.

Stool—occult blood test was positive, and it was acid in reaction.

Barium meal examination of the gastro-intestinal tract showed the presence of a large diverticulum arising from the second part of duodenum. The stomach and duodenal bulb were normal. The duodenal diverticulum contained barium residue at the end of 5 hours, though the stomach was completely empty (Fig. 1A and B, *vide* Plate) Cholecystography showed normal concentrating and contractile power of the gallbladder.

Case 2—R. M. K., Hindu male, aged 60 years, was admitted on 8-2-54 with copious haematemesis and melaena since 6-2-54. Both haematemesis and melaena stopped after 48 hours.

Since 1930, the patient was having dull pain in the epigastrium before meals which was relieved by food with periodic exacerbations and remissions. A few weeks before admission, the pain in the abdomen became more or less continuous. The patient had a similar attack of haematemesis and melaena in 1930. On admission, his blood pressure was 120/75 mm. of Hg.; pulse—84 per minute ; respiration—20 per minute ; temperature—98°F. No abnormality could be detected in the alimentary system on clinical examination. Stool examination showed presence of occult blood. Fractional test meal showed absence of free acid in the first examination—but that was not histamine-fast. Blood was present in all the samples and bile from the 3rd sample onwards in both instances.

Barium meal examination of the stomach and duodenum showed presence of a diverticulum arising from the 2nd part of duodenum ; stomach and duodenal bulb were normal. No residue of barium was detected in the diverticulum at the end of 5 hours (Fig. 2A and 2B, *vide* Plate).

Discussion

Both patients had been suffering from epigastric pain and discomfort for several years. Case 2 gave an interesting history of exacerbation of epigastric pain, a few weeks before the attack of haematemesis and melaena and also of a past attack of haematemesis and melaena 24 years back.

As both the cases presented otherwise normal appearances of stomach and duodenal bulb, it is reasonable to assume that bleeding occurred inside the diverticulum.

The cause of haemorrhage in these two cases was not established as both refused operative interference.

Lahey (quoted by Whitmore, 1948) had two cases of haemorrhage from duodenal diverticula. In one the bleeding spot was found in the excised diverticulum and the pathological report was atypical gastric mucosa.

Summary

Two cases of duodenal diverticulum with haemorrhagic complications are presented and the probable causes of haemorrhage in a diverticulum discussed.

Acknowledgment

I am grateful to Dr. S. Mukerji, Professor of Radiology (Diagnostic) and Dr. M. N. Sarkar, Principal and Superintendent, Medical College and Hospitals, Calcutta, for permitting me to publish the hospital records.

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A CASE OF CHLOROMA

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Chloroma is a rare disease closely allied to, if not actually a variant of, leukaemia. It is characterised by the presence of greenish-coloured tumours in various parts of the body which have a particular predilection for bones

The disease is common in children and young adults. It is occasionally found in middle-aged people and rarely in infants.

The blood picture is that of acute leukaemia. The leucocyte count usually varies from 14,000 to 20,000 per c.mm. though occasionally it is within normal limits. Leucopenia is rare. The leucocytic changes are associated with anaemia and signs of red cell regeneration.

A case of chloroma came under the observation of the authors. The case is reported :

Case Report

K. G., a 17 year old male, was admitted in the hospital on 21-1-55 for headache, pain all over the body and irregular fever for 4 weeks and bulging of the eyes with impaired vision and deafness for 3 weeks.

On examination—The patient was pale and anaemic, with proptosis and impaired vision of both the eyes, being more marked on the left than on the right (Fig. 1, *vide* Plate). The eyelids and conjunctivae were swollen and oedematous. Deafness in both ears was present. The spleen was enlarged 1″ below the costal margin and was firm. The liver was enlarged one inch below the costal margin and was firm but not tender. A haemic murmur was present. The pulse was 98 per minute and respiration 34 per minute. The blood pressure was 118/75 mm. of Hg. There was tenderness over all the bones of the body which was most marked at the lower end of the sternum. The following swellings were detected on the body :

a. Two swellings over the manubrium sterni one on each side of the middle line, the left one being slightly higher than the right, overlapping over the medial ends of the adjoining ribs, very firm, tender and fixed to the underlying bone each about 1¼″ in diameter (Fig. 1, *vide* Plate).

b. One swelling on the left temporal bone, very firm, fixed to the underlying bone, tender, about 1½″ in diameter.

c. A similar swelling 1″ in diameter situated on a similar site on the right temporal bone.

d. A small swelling ½″ in diameter situated on the frontal bone almost on the middle line.

Ophthalmoscopic examination of the fundus showed congestion of the veins and blurring of the disc margins.

LABORATORY FINDINGS :

Blood—Hb.—5·1 g. per cent ; R.B.C.—2,100,000 per c.mm.; colour index—0·83 ; W.B.C.—48,000 per c.mm. with blast cells 85 per cent, myelocytes 1 per cent, polymorphs 1·5 per cent, lymphocytes 12 per cent, monocytes 0·5 per cent, and occasional eosinophil and a very few normoblasts ; platelets—1,25,000 per c.mm.; bleeding time—4·5 minutes ; coagulation time—4·5 minutes; E.S.R.—154 mm. in 1st hour (Westergren) ; W.R. and Kahn tests—negative.

Urine—Albumin—occasional traces ; excess of phosphates ; Bence Jones proteose—absent.

Stool—no abnormality.

Skiagram of the skull showed three small punched out areas of translucency on the skull (Fig. 2, *vide* Plate).

Biopsy report of the tissue taken from a swelling on the sternum—The tumour is green in colour and fades on exposure to air. Section shows large mononucular non-granular cells similar to immature cells seen in his blood picture.

Sternal puncture material (as far from tumour as practicable) had the following picture: Blast cells—76 per cent, neutrophilic myelocytes—1 per cent, lymphocytes—12 per cent, neutrophilic polymorphonuclear cells—4 per cent, late normoblasts —7 per cent.

Progress of the patient—The condition of the patient progressively got worse. Bulging of the eyes increased very rapidly so much so that he was unable to close the eyelids and very little vision was left in the course of a few days. Deafness also increased. Pain particularly in the head was very severe. He was treated with iron, preparations of liver extract, penicillin, multivitamin tablets, analgesic drugs, etc.

Examination of the blood on subsequent days did not show much alteration.

The patient was taken away from the hospital on 25-5-55. The patient ultimately died at home in course of a few days.

Discussion

The diagnosis was suggested by the clinical picture of tumours on bones of the skull and sternum, exophthalmos, impaired vision, deafness, hepatosplenomegaly, anaemia, etc. The diagnosis was confirmed by the blood picture, biopsy of tumour and sternal puncture.

The two features in this particular case which may be of some interest are:

1. Three small punched out areas of translucency on the skull as revealed by x-ray. The picture is similar to what is seen in myeloma.
2. Somewhat symmetrical distribution of tumours on the two sides of the body, such as, within the orbits, on the manubrium sterni and on temporal bones. The tumour on the frontal bone was in the middle line.

Summary

A case of chloroma which is a very rare disease has been reported. It was myeloid in nature, very rapidly progressing and ending in death in course of 5 weeks.

Two features deserving more than a passing notice in this particular case were small punched out areas of translucency in the skull and somewhat symmetrical distribution of the tumours on the body.

Acknowledgments

I wish to express my thanks to Dr. S. K. Banerjee, Assistant Professor of Pathology, Calcutta Medical College, who kindly performed the examination of blood slides, sternal smears and biopsy material. My thanks are also due to Dr. S. Bhattacharji and other doctors of Raniganj Paper Mills for referring the case to me.

CRUVEILHIER-BAUMGARTEN SYNDROME

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This condition was first observed by Pegot (1833) in a patient having dilated tortuous veins on the abdominal wall with formation of caput medusa, and a murmur over the dilated veins on auscultation. Cruveilhier (1852) on necropsy of this case found a small non-cirrhotic liver, enlarged spleen, and a patent umbilical vein. Baumgarten (1908) reported a similar case characterised by distended abdominal veins, enlarged spleen, ascites, leucopenia, small atrophic liver, and a patent umbilical vein.

Armstrong *et al* (1942) reviewed 55 known cases and classified them into two groups. The first, called the Cruveilhier-Baumgarten 'disease', was featured by portal hypertension, splenomegaly, abdominal venous hum, small atrophic liver with little or no fibrosis, and a patent umbilical vein. Portal hypoplasia was thought to be the fundamental lesion in this group. The second group, termed Cruveilhier-Baumgarten 'syndrome', was characterised by portal hypertension, splenomegaly, umbilical collateral circulation, and a venous hum over the umbilical or xiphoid area. Cirrhosis of the liver was the predisposing cause of portal hypertension in most of the 49 cases in this group. Patent umbilical vein was present in only 8 cases belonging to this group.

Jahnke *et al* (1954) for the first time treated 3 cases of 'syndrome' by porta-caval shunt and with success. They described the venous hum as continuous in nature, being at times accentuated during systole, inspiration, or straining. Leucopenia and eosinophilia are mentioned as additional features of this condition.

Case Report

D. C. R., male, aged 12 years, was admitted in the Medical College Hospitals, Calcutta, on 14-1-55, with a history of irregular fever and an enlarging mass on the left side of the abdomen for the last six years, and generalised abdominal enlargement for the last three years. His parents, brothers and sisters were healthy.

On examination, he had slight anaemia, pallor and emaciation. Temperature was 99·5°F, pulse 100 per minute, and respiration 24 per minute. B.P. was 100/70 mm. of Hg. The abdomen was protuberant. Ascites was present. The spleen was ten fingersbreadth below the costal margin on the left midclavicular line. It was smooth and hard but not tender. Upper border of the splenic dullness was in the 5th interspace on the left mid-

axillary line. The liver was not palpable, and the upper border of the liver dullness was in the 4th interspace on the right midclavicular line. There was a circular venous pool, ½" in diameter, on the midline midway between the umbilicus and the xiphisternum, presenting a continuous thrill and murmur, accentuated during inspiration and coughing. Communicating with this pool there were distended veins on the upper abdomen and chest, flowing from below upwards. No veins were visible below the pool. The cardiac impulse was in the 3rd interspace just outside the left midclavicular line and was forceful. A soft systolic murmur was present in the mitral and pulmonary areas. The breath sounds were harsh all over the chest but diminished at the bases.

Investigations: Hb—10·19 g. per cent, R.B.C.—2·62 mill/c.mm., W.B.C.—1,500/c.mm. with neutrophils 57 per cent, eosinophils 8 per cent, monocytes 3 per cent and lymphocytes 32 per cent; reticulocytes 3·5 per cent.; thrombocytes—78,600/c.mm. M.C.V.—116·4 cubic microns, M.C.H.C.—33·2 per cent; E.S.R.—41 mm. per hour (Westergren); prothrombin time—24 sec.; bleeding time—2½ minutes; clotting time—1½ minutes; total protein—6·82 g. per cent with albumin 3·52 g. per cent and globulin 3·30 g. per cent; van den Bergh reaction—indirect positive; bilirubin content—0·4 mg. per cent; urea—28 mg. per cent, N.P.N.—25 mg. per cent. Blood sugar (half an hour after ingestion of 25 g. of glucose in water): blood from antecubital vein—140 mg. per cent, blood from venous pool—185 mg. per cent; W.R.—negative; C.F.T. for kala-azar—negative.

The myelogram showed a slightly increased erythropoiesis with presence of iron deficiency normoblasts. Stools and urine showed no abnormality. Ascitic fluid contained mostly endothelial cells. Venous pressure: antecubital veins—80 mm. of water; venous pool—200 mm. of water.

Biopsy—The liver tissue obtained by biopsy showed some increase in fibrous tissue of the portal tract with some inflammatory cells (Fig. 1, *vide* Plate). Liver cells had a clear swollen appearance. There was some evidence of regenerative changes in the liver cells.

Treatment—The patient responded well to rest and nutritious diet along with alkaline mixtures and haematinics. The temperature came down to normal in a few days, the anaemia improved, and ascites gradually diminished and disappeared. On 9-8-55 he vomited blood twice and was treated with blood transfusion.

On 13-9-55 a splenectomy was performed but, as the condition of the patient deteriorated during the operation, splenorenal anastomosis could not be done. The liver was seen to be small, shrunken deep under the ribs, and had a few nodules on the inferior surface. A patent umbilical vein was present. Spleen was very large, presenting a picture of congestive splenomegaly under the microscope.

Comments

The site of the venous hum midway between the umbilicus and the xiphisternum is rather unusual. The comparatively high sugar content of blood in the venous pool after a glucose feed shows its connection with the portal circulation. The venous pressure in the pool (200 mm. of water) is indicative of portal hypertension. Normal portal pressure was estimated by Blakemore (1948) as varying between 85 and 150 mm. of water. Haemogram and myelogram confirm the presence of hypersplenism. The slight degree of fibrosis in the liver does not seem to be sufficient to explain the portal hypertension in this case, and might well be secondary to atrophy of the liver due to portal hypoplasia with a patent umbilical vein. Jahnke *et al* (1954) did in fact express the view that fibrotic changes in the liver might be secondary to portal hypoplasia and not the result of acquired liver pathology. We, therefore, think that this case may be a 'Cruveilhier-Baumgarten disease', as classified by Armstrong *et al* quoted in the *J.A.M.A.* (1954). The clear swollen appearance of the liver cells might be due to their glycogen content, as the patient received a liberal supply of glucose prior to liver biopsy.

Summary

A case of Cruveilhier-Baumgarten syndrome is reported and discussed with reference to literature.

Splenectomy was done. Splenorenal anastomosis could not be done.

Acknowledgments

We are grateful to Dr. M. N. Sarkar, Principal cum Superintendent, Medical College and Hospitals, Calcutta, for permission to report this case. Our thanks are due to Dr. A. K. Duttagupta, Assistant Professor of Surgery, Medical College, Calcutta, for the surgical part of the treatment, and to Dr. D. Gooptu for valuable help in the investigations.

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FIBROUS DYSPLASIA OF THE MAXILLA

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'Fibrous dysplasia' is a bony lesion in which the normal osseous structure is replaced by fibrous tissue with a characteristic osteogenic tendency, forming non-laminated osteoid bone. The lesion usually develops centrally in the bone marrow and as it enlarges it distends or invades the cortex. The affected bone contains whitish or brownish areas of firm rubbery tissue which may vary in size. The tissue is gritty in consistency due to interposed osseous fragments.

The largest concept of fibrous dysplasia is based on the assumption that it is a hamartoma or tumour originating in the developmental tissue defects, which if it exists in a single bone gives rise to the monostotic variety and if in many bones, to the polyostotic variety.

A case of fibrous dysphasia of the maxilla is reported.

Case Report

The patient, a boy of 12 years, had a swelling arising from the left maxilla protruding outside and also intra-orally causing expansion of the alveolar margin (Fig. 1, *vide* Plate). The tumour was of the size of a big orange and was of firm consistency. For about a year and a half it was noticed as a small swelling following extraction of a tooth. From the beginning it was painless. Except for the facial disfigurement, it was not in any way troublesome to the patient.

Investigation—Skiagram revealed only a soft tissue swelling arising from the maxilla with areas of density here and there.

Biopsy report—Fibrous tissue with occasional calcified spots.

Treatment—The tumour was excised with excellent result. The residual facial disfigurement (Fig. 2, *vide* Plate) was not very embarrassing to the patient.

A CASE OF MYOPATHY

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AND
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A boy, aged nine years, was admitted on 30-5-1956 to the District Hospital, Chitaldurg, for difficulty in walking.

The father of the boy reported that he had six children, five boys and one girl, of whom four were living and two dead. The first two were boys who developed muscular weakness at about their eighth year, which gradually progressed to a fatal termination in their fifteenth year. The third issue was a girl who also developed a similar complaint as her elder brothers at her eighth year and had become now, at her fifteenth year, an absolute cripple unable to stand or sit and her death was expected any moment.

The present case developed muscular weakness at the same age as the others, viz., the eighth year of life. The first symptoms noticed were that he walked clumsily and frequently fell down. Then the weakness of the muscles became progressive day by day and the boy could walk with very great difficulty.

The boy gave sharp replies to questions asked of him. His intellect was normal. He exhibited marked lumbar lordosis (Fig. 1, *vide* Plate). There was tilting of the pelvis downwards on the right side and so the right lower extremity looked apparently longer and slightly abducted. Both the scapulae were winged. The ribs were standing out prominently. When the boy stood he did so awkwardly with feet wide apart. The feet were flat. Walking was very difficult and the gait was waddling in character. The manner in which the boy rose from the supine to erect position (Fig. 2, *vide* Plate) was characteristic and pathognomonic of primary muscular dystrophy.

There was wasting of the biceps, triceps, brachioradialis, pectoralis major, latissimus dorsi and trapezius muscles, as also the flexors of the hip, extensors of the knee and the glutei muscles. The boy could not raise the arms or flex the thighs or extend his knees. The knee, ankle, triceps and biceps jerks were diminished. There was no sensory change of any kind. Sphincters were not affected in any way. No fibrillations could be elicited in the affected muscles. Radiographs of the hip joints and shoulder joints did not reveal any abnormality. The wasted group of muscles suggested the disease as Erb's juvenile form of muscular dystrophy.

Though the diagnosis was obvious, the case is of interest for the following reasons:

1. The two elder brothers and an elder sister of the patient were victims of the same disease.

2. In all of them the disease appeared about the eighth year of life and progressed to a fatal termination in about seven years.

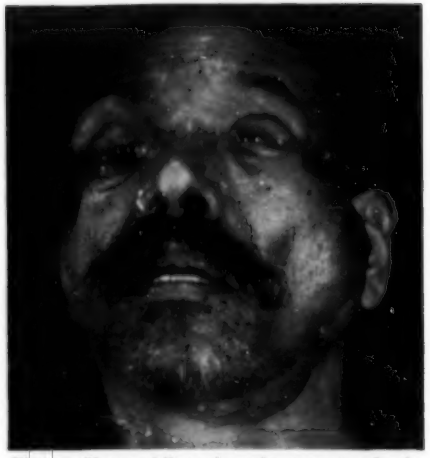

Fig. 1—Shows bilateral enlargement of the parotid, submandibular and lacrimal glands.

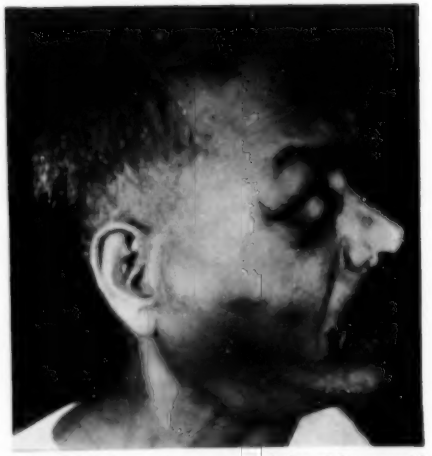

Fig. 2—Shows enlargement of the right parotid and submandibular glands.

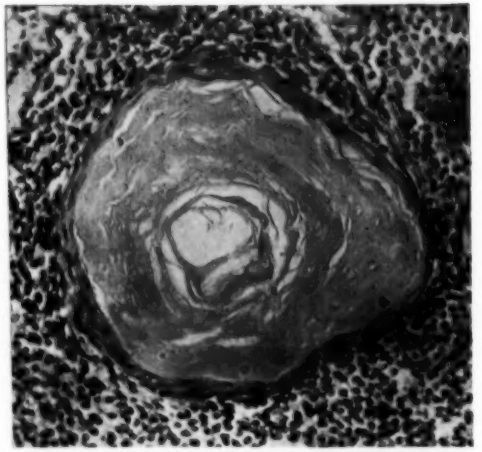

Fig. 3—Illustrates the typical myo-epithelial island surrounded by round cells. (H & E × 500)

RAGHAVACHAR ET AL—*Miculicz's Disease (p. 177)*

Fig. 1A

Fig. 1B

Fig. 1A—Diverticulum arising from the second part of the duodenum (marked by arrow). Fig. 1B—Shows barium residue in the diverticulum at the end of 5 hours.

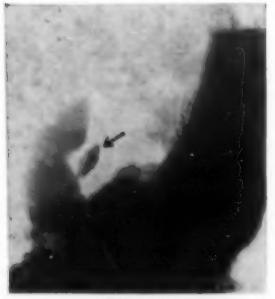

Fig. 2A

Fig. 2B

Fig. 2A and 2B—Diverticulum arising from the second part of the duodenum, marked by arrow.

BANERJEE—*Haemorrhagic Complications of Duodenal Diverticula (p.178)*

Fig. 1—Showing bilateral proptosis and two swellings over the manubrium sterni.

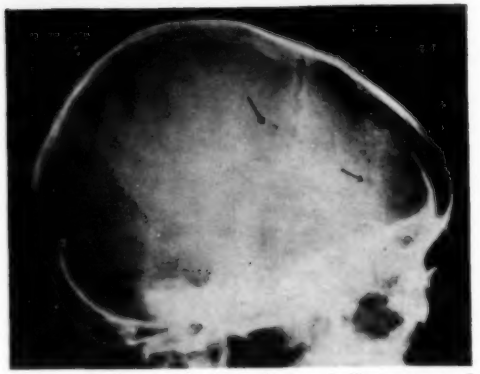

Fig. 2—Skull—lateral view. Arrows indicate areas of transluscency.

MUKHERJEE AND GHOSE—*A Case of Chloroma (p. 179)*

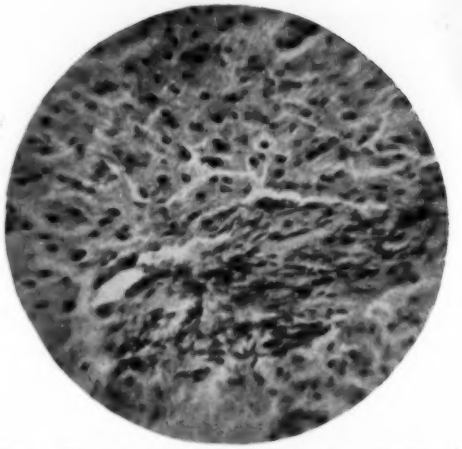

Fig. 1—Showing inflammatory cells in and around portal tract and increase in fibrous tissue. (H. & E. × 720)

BANERJEE ET AL—*Cruveilhier-Baumgarten Syndrome (p. 180)*

Fig. 1—Showing the position of the tumour.

Fig. 2—Facial appearance after removal of the tumour.

GOPALARAJAN AND SETTY—*Fibrous Dysplasia of the Maxilla (p. 182)*

Fig. 1—Showing lumbar lordosis.

Fig. 2—Showing characteristic manner of assuming the erect position.

APPAJAPPA AND SHAMANNA—*A Case of Myopathy (p. 182)*

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CALCUTTA, SEPTEMBER 1, 1956

THE PARATHYROID GLANDS

The increasing importance of parathyroid glands in recent years cannot be overemphasized, and their role in various clinical syndromes is being widely accepted. The first classical description of von Recklinghausen's disease in 1891 failed to correlate the aetiological relationship of parathyroid dysfunction. This relationship was for the first time recognised in 1923.[1]

The normal parathyroid gland occurs as small oval, brownish yellow glands usually 4 in number but sometimes varying from 2 to 12 in number, situated on the posterior aspect of the thyroid gland. Each gland is enveloped in a capsule penetrating the substance of the glands in the form of trabeculae which divide the parenchymal tissue in islets of cells. The parenchymal cells are mainly of 2 types, chief and oxyphil. The chief cells which are more numerous, consist of either pale, water clear wasserhelle cells with small round nuclei and abundant clear faintly staining cytoplasm. The smaller dark chief cells have less clear cytoplasm. The chief cells are arranged in anastomosing cords or in follicles with a mass of colloidal material in the lumen. The oxyphil cells are larger than the chief cells and have deeply staining nuclei embedded in dark cytoplasm. Glycogen is often present in the chief cells with occasional fat droplets in the cytoplasm[2].

The exact chemical composition of parathyroid hormone is unknown though it appears to be composed of protein and free amino acids. In health it is intimately connected with maintenance of the level of calcium and phosphorus ions in the blood in a fully saturated condition. The solubility product of calcium and phosphate ions is kept constant by the hormone. The actual mechanism of this control is still disputed though experimental evidence suggests either a direct action of the hormone on osteoclastic activity of the bone resulting in lacunar absorption[3], or the hormone acts on serum phosphate lowering its renal threshold[4]. The increased excretion of phosphates in the urine with resultant fall in the serum level, disturbs the solubility constant, so that calcium is mobilised from the bones leading to hypercalcaemia. The excess of calcium is excreted in the urine. The increase in the level of alkaline phosphatase in the blood is explained as due to increased osteoblastic activity to replace the absorbed bone by new organic matrix. Dent[5] considers the action of the hormone, to be direct on the bone as well as on the renal tissue leading to increased excretion of phosphates in the urine.

Disturbances in the function of parathyroid hormones result in syndromes of hypoparathyroidism or hyperparathyroidism.

Hypoparathyroidism usually follows accidental removal of the parathyroids in operation for thyroidectomy. The condition is rarely met with in clinical practice in idiopathic form which results either from total absence of the parathyroid tissue congenitally[6] or rarely due to replacement of the glandular tissue with fat[7]. It is reported

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[1] DAWSON, J. W. AND STRUTHERS, J. W.—*Edinburgh M. J.*, **30** : 421, 1923.

[2] ERDHERM, J.—*British Z. Path. Anat. U.Z. Allg. Pathol.*, **33** : 158, 1903.

[3] THOMPSON, D. L. AND COLLIP, J. B.—*Physiol. Rev.*, **1** : 309, 1932.

[4] ALBRIGHT, F. AND REIFENSTEIN, E. C.—*Arch. Int. Med.*, **62** : 199, 1948.

[5] DENT, C. E.—*Proc. Roy. Soc. Med.*, **46** : 291, 1953.

[6] DRAKE, T. G., ALBRIGHT, F., BAUR, W. AND CASTLEMAN, B.—*Ann. Int. Med.*, **12** : 175, 1939.

[7] CANTAROW, A., STEWART, H. L. AND MORGAN, D. R.—*Endocrinol.*, **24** : 556, 1939.

to be associated with widespread moniliasis[8]. Clinically the condition is characterised by increased neuromuscular irritability due to hypocalcaemia and by trophic changes in the ectodermal tissues such as loss of the hair and the nails and the development of cataract. The rarer manifestations of papilloedema and fits have been described[9]. A similar type of picture is met with in pseudohypoparathyroidism due to failure of end organs to utilise the normal quantity of hormones. The condition is differentiated from the primary hypoparathyroidism by inability to induce phosphate diuresis after injection of the parathyroid extract. Widespread skeletal demineralization has been reported[10], along with short stature and thick build as accompanying features. Familial idiopathic hypoparathyroidism in three brothers is reported[11]. Both the parents had normal parathyroid function, hence the condition was proposed to be due to a recessive hereditary factor.

Hyperparathyroidism results from excessive function of the parathyroid hormones and with few exceptional cases, occurs due to adenomas. The chief effects occur on the skeleton and the kidneys. In the former, symptoms occur as a result of osteoporosis of the bones, the severity depending upon the duration of hyperparathyroidism. The classical description of von Recklinghausen's disease occurs in the later stage characterised by subperiosteal resorption of the bones specially the clavicle, the ribs and the mandible. The affected bones are swollen, extremely porous and soft with few irregularly distributed areas of density indicating an attempt at new bone formation. The absence of lamina dura in the mandible as the earliest manifestation of the disease is stressed[4]. Renal changes consist of polyuria due to excess of calcium and phosphates in the urine. These changes may be preceded in 84 per cent cases by renal calculus before any characteristic bony lesions develop[12]. General symptoms like constipation, lassitude and weakness, are attributed to hypercalcaemia. Calcification of the cornea resulting in "band keratitis"[13], and diminished auditory acuity improved by parathyroidectomy[14] has been described. Metastatic calcification occurring in the tubular basement membrane of the kidney, and media of the vessels may be spotted by radiological means. A case of bilateral calcification of the basal ganglia of the brain as a result of metastatic calcification has been described[15]. Primary hyperparathyroidism invariably follows neoplastic condition of the parathyroids though rarely it occurs as idiopathic hyperplasia of one or all parathyroids. The latter has been explained to arise in response to excessive release of the pituitary parathyroid hormones[16].

Amongst the tumours the parathyroid adenoma is by far the commonest. Adenoma is usually single affecting the upper pair of the gland with greater frequency[17]. Rarely it is aberrent in position, found in the mediastinum, within the thyroid glands or behind the oesophagus. It is well circumscribed, encapsulated, brown in colour due to absence of fat, and varies in size from a pinhead to as much as 300 g. in weight. Histologically there is hyperplasia of the chief or oxyphil cells with great pleomorphism in size and shape of individual cells and scantiness of connective tissue with loss of fat tissue. Giant cells are not infrequently

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[8] ALBRIGHT, F., BURNETT, C. R., SMITH, P. H. AND PARSON, W.—*Ibid*, **30** : 922, 1942.

[9] GRANT, D. K.—*Quart. J. Med.*, **22** : 243, 1953.

[10] REYNOLDS, T. B., JACOBSON, G., EDMONDSON, H. A., MARTIN, H. E. AND NELSON, C. H.—*J. Clin. Endocrinol*, **12** : 560, 1952.

[11] GOLDMAN, R., REYNOLD, J. L., CUNNINGS, H. R. AND BASSET, S. H.—*J.A.M.A.*, **150** : 1104, 1952.

[12] CHUTE, R.—*J. Urol.*, **41** : 762, 1939.

[13] COGAN, D. E.—Quoted by Albright and Reifenstein (1948).

[14] TURNBULL, H. M.—Quoted by Baired, M., Grainger, R. and Rowland, B. C.—*Brit. J. Surg.*, **42** : 140, 1954.

[15] MEDILL, E. V.—*Brit. J. Radiol.*, **24** : 685, 1951.

[16] CHURCHIL, E. D. AND COPE, O.—*Ann. Surg.*, **104** : 9, 1936.

[17] NORRIS, E. H.—*Internat. Abstr. Surg.*, **84** : 1, 1947.

encountered. Oxyphil adenoma is relatively rare and its occurrence in women over 45 years of age has been described in detail with case reports of 6 patients[18], and in 3 cases with 2 tumours each[19].

Similarity between the picture of adenoma and sarcoidosis of the bone is very well discussed[20]. The points include radiological appearance, hypercalcaemia and increased level of phosphorus and alkaline phosphatase. The differentiating feature in sarcoidosis was inverted albumin-globulin ratio in the blood, which is normal in hyperparathyroidism. Two cases of sarcoidosis which closely resembled symptoms of hyperparathyroidism have been reported[21].

Neurologic symptoms complicating adenoma[22] and increasing frequency of association of peptic ulcer with adenoma has been recently mentioned[23, 24]. A case of adenoma of the parathyroid associated with osteitis fibrosa cystica has been reported[25].

Carcinoma of the parathyroid glands is being more frequently diagnosed as a cause of primary hyperparathyroidism. The correct diagnosis depends upon critical evaluation of both clinical history and histological findings. Only 4 cases of carcinoma in a study of 148 tumours has been found and fibromatous inflammatory reaction surrounding the tumour and its adherence to the adjacent tissue as a reliable criterion of malignancy has been mentioned[26]. Malignancy in a tumour can only be suspected when the extension of the tumour to the skin or the lymphnodes is apparent. Metastasis occurs by direct extension or through invasion of the lymphatics. Blood vessels are rarely invaded hence there is scarcity of metastasis to distant organs. A case of parathyroid carcinoma metastasising in the lymph nodes long after local extirpation of the tumour has been reported[27]. The removal of this lymph node again restored the blood chemistry to normal limits with remarkable improvement in the clinical condition. Metastasis has been described also by certain workers[28, 29].

Secondary hyperparathyroidism is met with as a result of disturbance in serum calcium and phosphorus levels in diseases like renal rickets, osteomalacia and metastatic new growths in the bones. Experimentally its production is successfully reported by repeated injections of phosphates[30]. The characteristic features have been described[31]. The hyperplasia affects all the glands to a minor degree. The glands are creamy grey in colour in contrast to brown colour of adenoma. They are less firm than adenomas and carcinomas. Microscopically the notable features are the uniform hyperplasia of chief cells with a tendency to vacuolation of the cytoplasm. The amount of stromal fat and connective tissue tends to diminish. Lastly, the parenchymal cells align in follicular pattern and the glycogen content is greater than found in any other condition.

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[18] SOMMERS, S. L. AND YOUNG, T. L.—*Am. J. Path.*, **28**: 673, 1952.

[19] TURNBULL, H. M. AND HUNTER, D.—Quoted by Willis, Pathology of Tumours. 1948 Edition.

[20] SALMON, H. W. AND MEYNELL, G. G.—*Brit. M. J.*, **2**: 1440, 1951.

[21] KLATSKIN, G. AND GORDON, M.—*Am. J. Med.*, **15**: 484, 1953.

[22] BOWERS, C. R. AND SHANNON, M. B.—*A.M.A. Arch. Surg.*, **66**: 695, 1953.

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[27] GENTILE, R. J., SKINNER, H. L. AND ASHBURN, L. L.—*Surgery*, **10**: 793, 1941.

[28] HALL, E. M., *et al* (1934)—Quoted by Anderson, W. A. D. Text Book of Pathology, Second Edition, 1953.

[29] BURKE LLOYD, B. (1947)—*Ibid.*

[30] DRAKE, T. G., ALBRIGHT, F. AND CASTLEMAN, B.—*J. Clin. Invest.*, **16**: 203, 1937.

[31] CASTLEMAN, B. AND MALLORY, T. B.—*Am. J. Path.*, **13**: 553, 1937.

CURRENT MEDICAL LITERATURE

Headache as a Symptom of Masked Epilepsy

HEYCK AND HESS (*Schweiz. med. Wschr.*, **85** : 573, 1955, Ref. *German M. J.*, **1** : 34, 1956) write :

Electroencephalograms were taken of a total of 48 patients with typical migraine and of 200 patients with persistent violent vasomotor headache (cephalaea vasomotorica). Normal electroencephalographic records were found in 50 per cent of the cases of migraine, 20 per cent of the cases showed non-specific general dysrhythmias, and a further 8 per cent focal disturbances. Paroxysmal hypersynchronism was found in 8 cases (16·6 per cent), usually in the shape of high, slow theta waves and so-called spike waves, such as are observed in clinical epilepsy. Similar changes in the electroencephalogram were demonstrated in the case of 20 patients with cephalaea vasomotorica. A series of other vaso-vagal seizures was displayed clinically by these patients. While no hereditary relationship with typical forms of epilepsy could be deduced, the good effect usually produced by anti-epileptic therapy pointed to its connection with the epileptic group of diseases.

Bacterial Flora of Throat in New-born Babies

BUCH AND JHALA (*Indian J. Child. Health*, **5** : 1, 1956) from an analysis of the results of cultural examination of the throat swab of new-born babies during various intervals of time observe :

Certain bacteria such as non-haemolytic streptococci and staphylococci appear very early and regularly in large numbers. These, therefore, may be assumed to possess a high degree of inherent adaptation to growth on this particular region. Others such as alpha-haemolytic streptococci, pneumococci and Neisseria, taking time to colonise probably have a lesser degree of inherent adaptation to the growth, thereby requiring more time and 'heavy inoculum' to get established as an integral part of the basic flora.

Treatment of Hepatic Coma after Viral Hepatitis in Infancy

BENAVIDES AND OTHERS (*Pediatrics*, **15** : 586, 1955, Ref. *Abs. World Med.*, **19** : 16, 1956) from an analysis of sixteen cases of hepatic coma out of 82 children suffering from viral hepatitis observe :

Careful biochemical and haematological examinations were carried out daily. Treatment, which was given in two stages, consisted chiefly in administration of corticotrophin and glutamic acid. During the first stage, which lasted 2 days or until consciousness returned, oral feeding was prohibited, the patients being given glucose solution containing corticotrophin and glutamic acid and also antibiotics intravenously and electrolytes parenterally. After this stage a liquid diet was permitted, administration of corticotrophin, glutamic acid, and electrolytes being continued. Of the 16 patients, 4 recovered, this being attributed partially to the combined action of corticotrophin and glutamic acid which exert a favourable influence on mobilisation and utilisation of glucose and on the reservoir of hepatic glycogen." In the authors' view administration of sedatives is contraindicated in hepatic coma.

Chlorpromazine in Tetanus

KELLY AND LAURENCE (*Lancet*, **1** : 118, 1956) in dealing with the effect of chlorpromazine on convulsions of experimental and clinical tetanus observe :

Chlorpromazine and promethazine abolish the muscle spasm of experimental tetanus in rabbits.

These drugs probably act by depressing spinal-cord interneurones or brain-stem reticular formation.

Severe tetanus convulsions in a child were controlled by means of large doses of chlorpromazine alone.

Fractures of Childhood

RIEDEL (*German M. J.*, **1** : 24, 1956) gives below the summary of his observations on the diagnosis and treatment of fractures in childhood :

Fractures in childhood have a number of special features, e.g., damage to the epiphyses and greenstick fractures. Dislocations and deformities of the shafts of long bones are generally corrected within a relatively short time in children. Fractures in the epiphyseal region, however, often lead to serious and progressive deformities. The fracture most frequently found in the newborn is that of the shaft of the humerus during breech delivery. It is of great importance to recognise any injury to arteries or nerves occurring at the same time. These fractures, if immobilised under traction, as a rule unite perfectly. Proximal and distal epiphyseal separations of the humerus are treated in the same way. Fractures of the clavicle sustained during birth unite in perfect position under a figure-of-eight bandage. The most common birth injury to the lower extremities is transverse or oblique fracture of the femoral diaphysis. In differential diagnosis proximal or distal separation of the epiphysis must be considered. Traumatic hip dislocation in the newborn appears to be extremely rare. Osteopsathyroisis may be responsible for multiple fractures of the long bones in babies; but the genetically determined defects disappear after puberty. Another typical fracture in the young infant is the "spontaneous" fracture of the lower leg, occurring between middle and lower third of the tibia and fibula, due to congenital crus varum; because of a defect of bone formation there is interference with callus growth and pseudoarthrosis easily develop, in which case open surgical reduction is definitely contra-indicated. In small children greenstick fractures are a common occurrence. Because the strong, yet elastic periosteal sheath prevents lateral bone displacement, these generally unite well, Medullary nailing is generally contra-indicated in the treatment of fractures in children as it may interfere with growth. Shortening, even if it is considerable, can be adequately corrected by extension strapping or wire traction. The prognosis of all fractures in the vicinity of the elbow joint is relatively unfavourable. In all fractures of the long bones the neighbouring joints should be examined very carefully. In older children fractures of the 1st, 2nd or 3rd metatarsal may sometimes occur as the result

of excessive stress. In fracture separation of the epiphyses, most frequently in those of the distal end of the radius, deformity of growth often results. Their prevention and correction usually requires prolonged treatment. The treatment of fractures of the skull, upper and lower jaw and of the bones of the trunk should only be undertaken in close collaboration with a specialist surgeon, physician and neurologist. These victims of serious accidents often require very prolonged treatment.

Laurence-Moon-Biedl Syndrome

HOU-CHANG (*Chinese M. J.*, **74** : 75, 1955) in reporting on two cases of Laurence-Moon-Biedle syndrome observes that the two patients reported were brothers. Of the five symptoms of Laurence-Moon-Biedl syndrome, pigmentary degeneration of the retina, obesity, hypogenitalism and mental deficiency were present. The elder brother was obese, the younger brother was short and less obese. Neither of them showed polydactylism. They had curly hair, long eyebrows and long eyelashes, features not previously mentioned in the literature. Besides pigmentary degeneration of the retina there were changes resembling those of retinitis proliferans, of which there is yet no clinical explanation.

Gastrointestinal Haemorrhage in Elderly Patients

ALMY AND OTHERS (*Bull. N. Y. Acad. Med.*, **32** : 337, 1956) write that in elderly patients, gastrointestinal haemorrhage has a number of clinical consequences, which are related to the circulatory readjustments to a diminished blood volume. Compensatory reduction in renal or hepatic blood flow, if prolonged, may lead to acute renal or hepatic failure. Diminished blood flow in the extremities may result in arterial thrombosis and subsequent gangrene. With inadequacy of these compensatory mechanisms, the coronary or cerebral blood flow is reduced, and, particularly in the presence of localized atherosclerotic narrowing, myocardial infarction or a cerebrovascular accident may occur. Cases are cited to illustrate each of these eventualities.

In such cases, the replacement of blood must be adequate to relieve not only hypotension but also the indications of renal, hepatic, and peripheral vasoconstriction. In some cases emergency surgery may incur less danger for the patient than would continued, inadequately compensated bleeding.

Gastrointestinal haemorrhage in the elderly is largely a preventable catastrophe, as most uncomplicated cases of chronic peptic ulcer, hiatus hernia, and diverticulitis can be safely and effectively treated in early or middle life (*Authors' summary*).

Cirrhosis of the Liver

HOLZNER AND OTHERS (*German M. Monthly*, **1** : 92, 1956) in considering the aetiology and causes of death in 439 cases of cirrhosis of the liver (274 men, 165 women) collected from more than 24,000 autopsies performed during 1944-53 observe that hepatitis was found to be the most important aetiological factor of cirrhosis of the liver, followed by excessive alcohol intake, which in men was actually the most common cause. But in women posthepatitic cirrhosis was about 3 times more frequent than alcoholic cirrhosis. Obstructive and hypertrophic biliary cirrhosis affected both sexes in equal proportion. It was more frequent in the higher age groups. Posthepatitic, as well as alcoholic, cirrhosis had a peak incidence in people between the ages of 50 and 60 years. Cases of alcoholic cirrhosis did not occur in the under-30 age group. Acute or subacute hepatic coma was the most common cause of death in cirrhosis of the liver, particularly in women. Haemorrhages from oesophageal varices and circulatory failure were second and third, respectively, as the next most frequent causes of death. 18 patients had died of primary carcinoma of the liver.

Uncomplicated Syphilitic Aortitis

IRVINE (*Brit. M.J.*, **1** : 832, 1956) gives in the following lines the summary of his observations on the outcome of 61 uncomplicated aortitis in the course of the routine cardiological examination of 1330 syphilitic patients :

The diagnosis was made in the presence of a dilated ascending aorta, recognised at fluoroscopy. In seven cases the ascending aorta was also calcified.

These patients were observed at repeated intervals for periods of 3 to 14 years, with an average of 5·1 years.

For the first seven years after diagnosis the expectation of life in these patients was normal, but one died eventually of aortic incompetence after 14 years.

Progress to aortic incompetence or to further dilatation of the aorta occurred at a fairly constant rate and affected about a third of the patients after an average interval of three and a half years from diagnosis.

No factors of undisputable prognostic importance were discovered, but there was some evidence to show that those with symptoms at the time of diagnosis and those with the greater degree of aortic dilatation did worse than the others.

No appreciable prognostic effect could be attached to age, sex, occupation, the duration of infection, the presence of an aortic systolic murmur or accentuated second sound, the titre of the serum Wassermann reaction, or the amount of antisyphilitic treatment.

The significance of these findings is discussed.

Importance of Basal Blood Pressure

CALDWELL AND HOLLINGER (*Henry Ford Hosp. Med. Bull.*, **3** : 175, 1956) write that blood pressure in an individual varies widely under differing environmental conditions and as determined by different examiners. Basal blood pressure is a more constant and a more reproducible index of blood pressure levels than is the customary casual office readings as demonstrated by Kilpatrick.

A practical method for measuring the physiological minimum of blood pressure in the out-patient clinic or office is described. This is of importance because it enlightens both the physician and the patient by demonstrating the range of variability in blood pressure and the value of rest.

The patient is seen on appointment by a technical assistant expressly for the purpose of obtaining resting

or basal blood pressure. The attending physician is not seen at this visit or if so only in a casual manner. The patient is placed recumbent in a large warm and quiet room on a comfortable cot. The technician places a "Do Not Disturb" sign outside the door of the room, enters quietly and assumes a friendly and sedate manner toward the patient. Adjusting the sphygmomanometer she proceeds to record the blood pressure rapidly and frequently over the first three minutes to "desensitize the patient to the sphygmomanometry". Thereafter the blood pressure is determined every five minutes for a period of one-half hour. All blood pressure measurements are made on the same arm at heart level with the same mercury manometer using the method of judging systolic and diastolic level as detailed by the American Heart Association recommendations of 1951.

As done here it eliminates the pressor aspect of readings by the physician, although this can be achieved very simply by having a nurse or competent technician determine blood pressure at the time of routine office visits.

Basal blood pressure aids in separating "transient hypertensives" or "vascular hyperreactors" from those with sustained hypertension. It gives information regarding the "fixed level" and may prove to be of value in prognosis.

Noting a wide discrepancy between casual and basal levels in some patients with low basal levels, a physician may avoid enthusiastic overtreatment of "vascular hyperreactors". By determination of basal blood pressure before treatment one is in a better position to evaluate psychic factors as contrasted to truly pharmacologic effects of a drug used.

Its greatest value is its contribution to a more complete knowledge of the significance of blood pressure levels in an individual patient.

CURRENT TOPICS

DANGERS OF RADIATION IN INDIA

Professor J. B. S. Haldane, addressing a meeting organised jointly by the West Bengal Peace Council and Kalikata Yuba Sangha at Wellington Square, Calcutta, on the 5th August, 1956, spoke on the effects of atomic radiation on the human body. He said that when a thermonuclear or hydrogen bomb exploded well above ground level, radioactive particles rose 20 miles or more into the stratosphere, where they were harmless save for possible effects on the weather. They came down over many years as small particles of dust. These emitted radiations when on the ground and penetrated human tissue. Some were breathed in and might settle in the lungs, while others were swallowed directly or after the incorporation of radioactive atoms into food. One element—strontium—was incorporated into the bones especially bones which were growing quickly, "as in children and calves".

The radiation from exploding atomic nuclei could harm human beings in two different ways. They could cause damage within a life-time or by altering some components of the germ cells in men or women could cause illness or death in future generations. The British Government had recently issued a document on both these dangers.

From the amount of dust which has already fallen in Britain, British Government representatives have calculated the dose which would be received by a man in the open. But they "divide this by a factor of seven to allow for the protection given by brick and stone houses". This factor could not be applied to India. Most Indians spent much of their time in the open and lived in houses whose walls consisted of matting, which gave no appreciable protection. So, for a given amount of dust falling to the ground, the "danger is perhaps five times as great in India as in England. Secondly, in England most of the dust is brought down by rain and much is rapidly washed into the ground. In India radioactive dust settles during eight months or so when there is little rain".

So the results in India were considerably more serious. He said, Indian physicists had detected a fall of dust and radioactive substances in human food like vegetables. They had not yet published quantitative data. And this was an urgent task requiring dozens of trained men and women. The danger was certainly greater in India than in England.

According to Professor Haldane, the dangers to persons immediately exposed were not great. One of them was leukaemia, the disease of which Madam Joliot Curie, the discoverer of radium, and her daughter Madam Joliot-Curie died. So had died about 100 of the survivors of Hiroshima and Nagasaki and nearly 100 Britons who had had large doses of x-rays.

If atom bombs were let off for a generation at the same rate as during the last few years, he doubted if 100 Indians would die of this disease and a few hundreds of other diseases such as bone cancer, known to be caused by radioactive substances. But the dangers to posterity were vastly greater. The total number of cases of premature deaths in future generations would be several lakhs. Many of these deaths might be prenatal. There would also be a great deal of chronic illness and deformity.

This figure, Professor Haldane said, might be badly wrong. The Americans were doing research to answer this question. "Their research was deliberately designed not to do so". The British Government had also started research on this matter. He had worked out a method which had been adopted. He had full confidence in his colleagues who were carrying out his work in England. But he was not sure that the results would be published if unfavourable. He criticised his Government, but nevertheless he wished to say that his Government's record in this matter was better than that of America's. He said that he would be in Japan next month when he would try to persuade the Japanese biologists to use the method he had suggested. He would be happy if scientists in India did the same.

He thanked the Indian Government, especially Mr. Nehru and Mr. Krishna Menon, for the stand they had taken on the question of atom bombs. Some might not agree with this policy in all details, but all, he was

sure, would agree that it was a much better policy than that of the U.K. or the U.S.A. He wished his Government followed a similar policy as India's in the matter of hydrogen bombs.

It was of the utmost importance for the whole world to realise that whatever might be the case in other countries, the people of India were solidly behind the policy of peace.

POSTGRADUATE AND UNDERGRADUATE MEDICAL EDUCATION

Talking to a gathering of distinguished medical men in Calcutta on 10-8-56 on "Postgraduate and Undergraduate Medical Education", Prof. I. G. W. Hill, Professor of Medicine, Dundee, stressed that undergraduate teaching in medicine should be entrusted to a board of teachers distinguished as specialists.

Prof. Hill pointed out that undergraduate medical education should be aimed at producing doctors for serving people at large to relieve their general ailments. Those who wanted to qualify as specialists should go in for post-graduate education after some years of general practice. He strongly deprecated the idea of being a specialist without gaining sufficient experience as a general practitioner. Incidentally, he said that of five medical graduates one was expected to turn out a specialist later.

Referring to the much-talked-about postgraduate teaching in medicine, Prof. Hill said that they should proceed carefully. In institutions where both undergraduate and postgraduate teaching in medicine were available there should be some beds set apart for postgraduate teaching. The bedside approach for teaching was most important and clinical study should be done as thoroughly as possible.

As to medical education which was principally conducted at State expense in England, the selection of candidates for medical education, Prof. Hill said, was made strictly after a careful consideration of each individual case. It was a hard task to select only a few from so large a number of applicants as 1,600 to 1,700. He felt that students must possess certain pre-medical educational qualifications as also personality for undertaking the training. In any case, the teachers must have a large say in the final selection of candidates for admission. They had in Scotland 7 years' of medical education including one year's pre-medical study and another year's special training in medicine and surgery, during the last year. They had arrangements for 7 to 10 students for clinical study under a teacher.

Giving his own mind regarding research work in medical science Prof. Hill pointed out that not even one per cent professing medicine was expected to take up research work. Research workers were not made but those with a special knack for investigation would only be going to take up this special line. But all facilities for training in research methods should first be acquired by the workers, if needed, at State expense, he emphasised.

Replying to a query the speaker said that in Britain the Government made sufficient grants for educational purposes but nowhere education was State-controlled. From that angle educational bodies were independent. They felt that medical education should be under the care of a council of experienced medical men and not under the university control.

CONSTITUTION OF THE WORLD HEALTH ORGANIZATION

The following statement was released by Dr. M. G. Candau, Director-General of WHO:

Ten years ago, on 22 July 1946, representatives of 61 countries, assembled in New York City, signed the Constitution of the World Health Organization (WHO) which is dedicated to the attainment by all peoples of the highest possible level of health.

On the same day, the Interim Commission of the World Health Organization, consisting of persons designated by 18 States, was established and remained in being until, in 1948, the Constitution was ratified by 26 Member States thus bringing the World Health Organization officially into being as a Specialized Agency of the United Nations.

The foundation of the World Health Organization was thus laid ten years ago. A great deal has happened since. The Organization now has 84 full Member States and four Associate Members. It has established six regional offices in different parts of the world and now operates at a budget level of nearly $11,000,000. By 1956, it was estimated that some 400 million people, constituting one-sixth of the world population, had already benefited from modern methods of controlling malaria, tuberculosis and treponematoses as a result of programmes assisted by WHO. Apart from operating central technical services including a world-wide epidemiological intelligence service, WHO is now assisting more than 500 health projects in 108 countries and territories. A considerable proportion of those projects have been made possible through the assistance of the United Nations Children's Fund and further funds made available under the United Nations Technical Assistance Programme.

In the early years, following immediately upon the signing of the Constitution of WHO, progress was of necessity slow. However, at this milestone in the history of the Organization, it can be said that not only have sure foundations been laid, but that practical results of great importance to the future health of the world have already been achieved. In two years' time the World Health Organization will officially celebrate its tenth anniversary as an effectively operating agency with its own independent governing body and annual budget. This will be the moment to assess its achievements more fully.

In the meantime there are solid grounds for satisfaction in the progress made in the 10 years since the historic occasion of the signature of the Constitution, and in the fact that the objectives and inspiration of our work which are precisely laid down and defined in that blue-print remain of unimpaired validity today.

NOTES AND NEWS

Family Planning Board in Madras

In accordance with the policy laid down by the Government of India, the Madras Government have decided to constitute a Family Planning Board to propagate family planning methods during the Second Plan period. The Board will consist of four non-officials and seven officials and its functions would be to prepare and publish a family planning manual containing full information about the extent to which different methods of family planning are actually prevalent and give advice regarding the practice of those methods. The manual in particular would provide such information and advice as may be specially useful for married couples in low-income groups.

The Board will have a full-time Family Planning Officer on the executive side.

The Madras Government, in deciding to establish the State Family Planning Board, point out that they have decided actively to co-operate with the Government of India in the execution of the all-India policy and to secure propagation of practice of family planning in the State to the maximum extent practicable during the Second Plan period.

Medical and Public Health Institutions in West Bengal

Of late, a number of Advisory Committees have been appointed by the West Bengal Government to advise them on measures for the betterment of the existing facilities in this State for maintenance and improvement of the health of the people and also in the matter of improvement and progress of different medical and public health institutions in the State.

The following are the different committees :

Medical Relief Co-ordination Committee; Medical Education Co-ordination Committee; Advisory Committee, Medicine; Advisory Committee, Surgery; Advisory Committee, Obstetrics & Gynaecology; Advisory Committee, Pathology; Advisory Committee, Preventive and Social Medicine; Advisory Committee, Radiology (Diagnostic and Therapeutic); Advisory Committee, Ophthalmology & Otorhinolaryngology; Advisory Committee, Basic Medical Sciences, Anatomy, Physiology and Pharmacology; Public Health Advisory Committee; Scientific and Research Co-ordination Committee; Maternity and Child Welfare Committee; and Nursing Advisory Committee.

Congress of the International Society of Haematology and Blood Transfusion

The 6th international congress of the International Society of Haematology and Blood Transfusion is to be held in Boston from August 26th to September 5th, 1956. Dr. J. B. Chatterjea, Officer-in-charge, Haematology Research Department of the School of Tropical Medicine, Calcutta, will participate in the scientific deliberations on special invitation. He will present papers on Cyto chemical patterns of megakaryocytes and Cooley's anaemia. Dr. Chatterjea is a fellow of the International Society of Haematology and since 1952 the Councillor to the Society from India.

Dr. Chatterjea has also been invited to address the "Society for the Study of Blood" at the Mount Sinai Hospital, New York.

The First European Study Tour Sponsored by IMA

The Frst European Study Tour organised and sponsored by the Indian Medical Association with the co-operation of Messrs. Trade Wings Ltd., Travel Agents, started from Bombay on 21 August 1956 and will terminate at Bombay on 9 October 1956. An attractive itinerary has been arranged including visits to Italy, Austria, Switzerland, W. Germany, Belgium, Netherlands, England and France. Apart from sightseeing visits to places of cultural and historical interest, visits have also been arranged to important pharmaceutical manufacturing concerns, medical centres and hospitals and arrangements have been made for lectures and demonstrations on medical subjects through the kind co-operation of national medical associations in each of the countries. The following is the list of participants.

1. Dr. A. P. Mittra, Hony. General Secretary, I.M.A., Leader of the team, 2. Dr. V. N. Bhave, 3. Dr. S. R. Behere, 4. Mrs. Kamal S. Behere, 5. Dr. K. V. Chary, 6. Dr. K. N. Chandrasekharaswamy, 7. Mrs. Chandrasekharaswamy, 8. Dr. A. G. Chacko, 9. Dr. N. G. Desai, 10. Dr. K. A. Dhairyawan, 11. Dr. B. N. Ghose, 12. Mrs. Mira Ghose, 13. Dr. M. Gopala Pillai, 14. Dr. V. K. Kamath, 15. Mrs. Kamath, 16. Dr. S. B. Kirtane, 17. Dr. K. V. Krishnamurthy, 18. Dr. M. C. Kothary, 19. Mrs. Surajben Kothary, 20. Dr. D. R. Mandrekar, 21. Dr. J. J. Merchant, 22. Mrs. Lily Merchant, 23. Miss Usha J. Merchant, 24. Dr. K. Narayanamurthy, 25. Dr. N. P. Panikkar, 26. Dr. M. A. Paranjpe, 27. Dr. (Mrs.) Y. M. Paranjpe, 28. Dr. S. S. Pai, 29. Dr. K. V. Pai, 30. Dr. Vinayabai Pai, 31. Dr. I. D. Patel, 32. Dr. R. P. Patel, 33. Dr. B. B. Parab, 34. Dr. N. R. Pathak, 35. Dr. B. V. Rama Rao, 36. Dr. (Mrs.) Kamala Ramaier, 37. Dr. M. B. Raut, 38. Mrs. Malati M. Raut, 39. Dr. A. B. Sardeshpande, 40. Mrs. S. A. Sardeshpande, 41. Dr. S. K. Sengupta, 42. Dr. C. B. Shroff, 43. Mrs. C. B. Shroff, 44. Dr. A. C. Shah, 45. Mrs. Maniben A. Shah, 46. Dr. P. F. Soonawalla, 47. Dr. Sumant M. Shah, 48. Dr. A. S. Syed, 49. Dr. K. G. Thangamma, 50. Dr. N. H. Udwadia, 51. Mrs. P. N. Udwadia, 52. Dr. Jayantilal N. Vakil, 53. Mrs. Mandakini J. Vakil, 54. Dr. Kamalakant Varma, 55. Dr. V. N. Vaishnev, 56. Mrs. Panwalla, 57. Dr. (Miss) Malini Trilokekar, 58. Dr. J. L. Pandya, 59. Dr. J. W. Dhurandhar, 60. Mr. D. G. Telang and 61. Dr. M. A. Panwalla.

Tuberculosis Services in India

To train a sufficient number of personnel for tuberculosis services, the Government of India proposes to subsidise the establishment of about 15 T.B. demonstration and training centres in the country under the second Five Year Plan. These centres will provide training to T.B. workers of all categories and also demonstrate the latest techniques in the diagnosis and prevention of the disease.

Three such centres were established under the first Plan at New Delhi, Trivandrum and Patna. Two more centres are in the process of being established at Madras and Nagpur by the State Governments concerned with the assistance of W.H.O., which has been requested to provide similar assistance for two more centres at Agra and Hyderabad.

The centres to be established under the second Plan will consist of four main sections: (*i*) epidemiological section for mass x-ray and B.C.G. vaccination, (*ii*) clinical section for diagnosis and treatment; (*iii*) bacteriological section and (*iv*) domiciliary service section under the direction of a public health nurse.

There will be a wholetime director to supervise the working of all these sections. He will also be responsible for co-ordinating their work with a view to laying emphasis on the preventive aspects of the work.

Radiation Effect on Heredity

A group of 20 scientists from nine countries were to meet in Copenhagen early in August 1956 to try to fill in the main gaps in the present knowledge of the effects of radiation on human heredity.

The object of this meeting was to discuss recommendation of further research that might help towards answering the hitherto unanswered questions and to advise W.H.O. how it could most usefully assist in advancing and co-ordinating such research.

Although numerous investigations have been made on the genetic damage caused by radiation in animals, it is not clear how the information contained could be interpreted in terms of human heredity.

The organisation hopes, therefore, to obtain guidance from the study group concerning lines of research which may be expected to shed direct light on the effects of radiation on human genetics.

Countries taking part are: India, the U.S.A., the U.K., France, Canada, Denmark, Sweden, Bazil and Germany.

Drugs Sales Tax Reduced

With effect from August 1, drugs, patent or proprietary medicines and surgical dressing, including gauze, lint and cotton wool, which conform to the accepted standards of the medical profession have been brought under the operation of the West Bengal Sales Tax, 1954, and as a result, sales tax on these goods will be reduced from 9 pies in the rupee to 3 per cent of value or a little less than 6 pies in the rupee, and will be payable only by manufacturers and importers. Old stocks, except those with manufacturers and importers, will continue to be taxed under the Finance (Sales Tax) Act of 1941.

First Panamerican Congress of Gerontology

The first Panamerican Congress of Gerontology will be held at Mexico City on 15-22 September, 1956. This Congress is sponsored by the International Association of Gerontology and by all the affiliated societies of the American Continent. To facilitate the development of this Congress, it has been divided into two sections, 1. Medical-biological and research problems, 2. Social-economical problems. All enquiries regarding the Congress and travel facilities to Mexico may be addressed to Messrs. Thos. Cook & Son (Continental and Overseas) Ltd., Cook's Building, D. Naoroji Road, Bombay 1.

Bombay Medical Congress

The 14th Bombay Medical Congress will be held at the Taj Mahal Hotel on 25-26 November 1956 under the presidentship of Dr. K. G. Munsif. A small exhibition will be held at the time of the Congress Session.

Internships and Residencies in U.S.A. and Canada

As in previous years applications have been invited by the Hony. Joint Secretary, I.M.A., for internships and residencies in U.S.A. and Canada for 1957. The appointments usually commence from 1st July. The appointments ordinarily carry a stipend. Selected candidates will have to defray their own passage expenses. The specialities in which internships and residencies may be available, are:

1. Anaesthesiology, 2. Dermatology and Syphilology, 3. General Surgery, 4. Internal Medicine, 5. Neurology, 6. Obstetrics & Gynaecology, 7. Ophthalmology, 8. Orthopaedic Surgery, 9. Otolaryngology, 10. Pathology, 11. Pediatrics, 12. Psychiatry, 13. Pulmonary Diseases, 14. Radiology, 15. Rotating Internships (Medicine, Surgery, Midwifery, Pathology—roughly 3 months each).

REVIEWS

Cardiovascular Innervation—By Prof. G. A. G. Mitchell, O.B.E., T.D., M.B., CH.M., D.SC.; with foreword by Sir Geoffrey Jefferson, *emeritus* Professor of Neurological Survey in the University of Manchester. Board-bound, 10" × 7", 356 pages with 217 illustrations, many in colour, E. & S. Livingstone Ltd., Edinburgh and London, 1956. Price 55s. net.

In spite of our studies over centuries, works on anatomy of the nerve-supplies of the cardiovascular system are indeed very few and much of our knowledge of the autonomic nervous system is based on experiments on lower animals. Moverover, the subject of the innervation of the heart and vessels and also the possible central connections of the vital neurovascular complex is usually given scant consideration in well-known anatomical treatises. It is indeed difficult to find a complete and systematic account of the present knowledge on this subject. Professor Mitchell has brilliantly handled the voluminous literature on this subject, supplemented by his own meticulous experiments and observations—on man or animals not lower than the monkey. These materials form the basis of this excellent monograph which is primarily anatomical and concerned with man. But the neurovascular complex is indeed so vital in the animal economy that it cannot be dissociated from other relevant considerations. This monograph will prove highly interesting to clinicians and surgeons dealing with the cardiovascular system, as also make for itself a place as a reference book on the subject.

Synthetic Drugs—By H. Ronald Fleck. Published by Cleaver Hume Press Ltd., London, 1955, pp. 380. Price 70s.

Since the time of Wöhler's classical synthesis of urea the synthetic side of organic chemistry has made rapid strides. Success of this development has not only enriched chemistry but a good number of drugs have been presented to the medical world. During the last 100 years many outstanding therapeutic agents have been produced synthetically. From the time of synthesis of salicylic acid by Kölbe, researches in synthetic chemistry have definitely helped to bring physicians and chemists to come closer in their common aim to enhance scientific progress. The discovery of sulpha drugs, the isolation and synthesis of vitamins and last but not the least the recent developments in antibiotics have brought revolutionary changes in medicine, giving fresh and effective weapons in the hands of the physicians in their fight against disease and death. On the other hand, the researches in the medical world have put new demands on chemists to produce further synthetic therapeutic agents. The book is an excellent treatise on this subject and physicians, chemists, and pharmacists should be equally interested and benefited. It is definitely a good hand book on synthetic drugs. As a book of reference it will immensely help the workers in the teaching institutions and laboratories. Those carrying on commercial production of drugs will also get much benefit from it.

The drugs have been treated in 15 chapters with a supplement dealing with the recent work on antibiotics. The book contains a good selection of synthetic drugs covering all important groups. From amoebacides to vitamins, representative drugs are selected. The classification of drugs has been done on the basis of their actions. Each chapter dealing with a particular group of drugs, contains a general discussion introducing the classification from the medical point of view. The individual members are differentiated on the basis of their chemical nature. Structural formula of the drug and the chemical synthesis are discussed. Along with the chemical properties, analysis and test of the drug, doses and clinical uses are given in a summary form. The discussion on chemical structure and drug action has been introduced. Mention may be made of anti-histaminic, autonomic and anaesthetic agents in this connection. In case of anaesthetics the importance of *anaesthesiophoric* group, i.e., the di-alkyl-amino-alkyl group, has been stressed showing the importance of knowing structure and how this knowledge helps to prepare more synthetic agents. While the method of synthetic preparation of each drug is discussed, the original natural source and method of preparation is not missed. In this connection it may be mentioned that a reference bibliography would have been very helpful for the workers, who want to use this as a handbook. The indexing work is very good. The introduction of general and clinical index separately has added usefulness to the book. The only point against the book is in its high price.

OBITUARY

Dr. A. S. Barot, M.B.B.S.

Dr. Amritlal Somabhai Barot, Rao Bahadur, was born at Dahegam on 13th September 1899. He graduated from the Grant Medical College, Bombay in 1925 and started independent practice at Dohad in 1927.

DR. A. S. BAROT

Dr. Barot was a social worker and rendered invaluable services to the cause of humanity in times of famine. He was the President of the Dohad Municipality in the year 1930-36 and 1941-46. He laid the foundation stone of the badly needed Dohad Municipal Maternity Home.

Dr. Barot was the founder member of the Dohad Branch of I.M.A. and was its President from 1939 till 1952.

He died of cerebral thrombosis on 1 July 1956 at the age of 57, after a very brief illness.

May his soul rest in peace!

VII HYDERABAD STATE MEDICAL CONFERENCE, AURANGABAD, 1956

The Seventh Hyderabad State Medical Conference will be held at Aurangabad on 23-25 September 1956. There will be a Scientific Session and an Industrial Scientific Exhibition. Aurangabad is an international tourist centre, on account of Ellora, Ajanta Caves and other historical monuments. Particulars may be had from the Secretary, VII Hyderabad State Medical Conference, Aurangabad.

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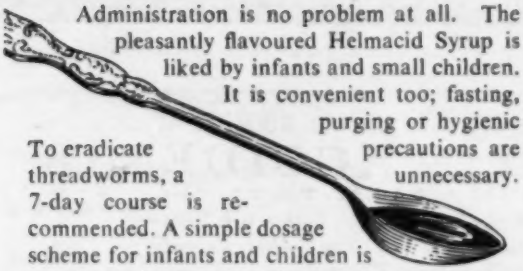

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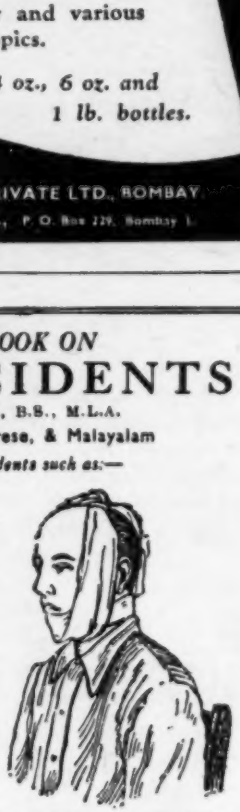

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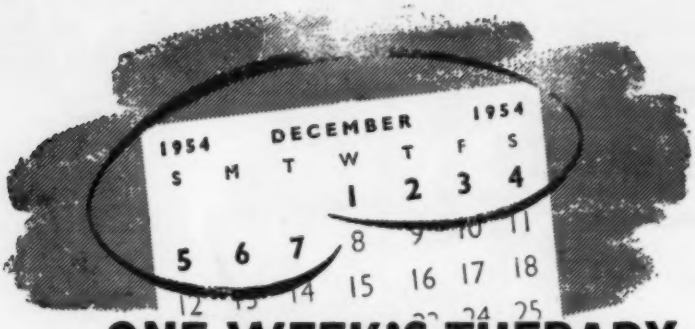

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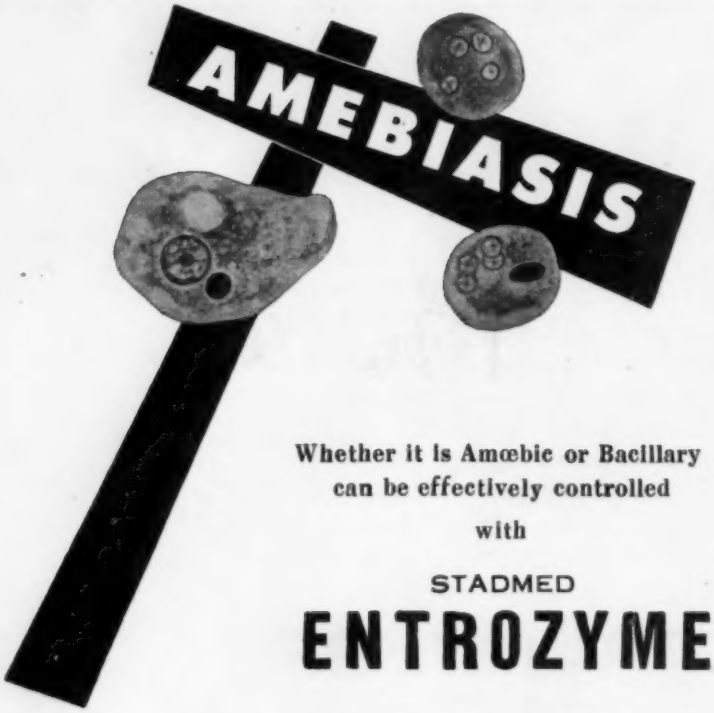

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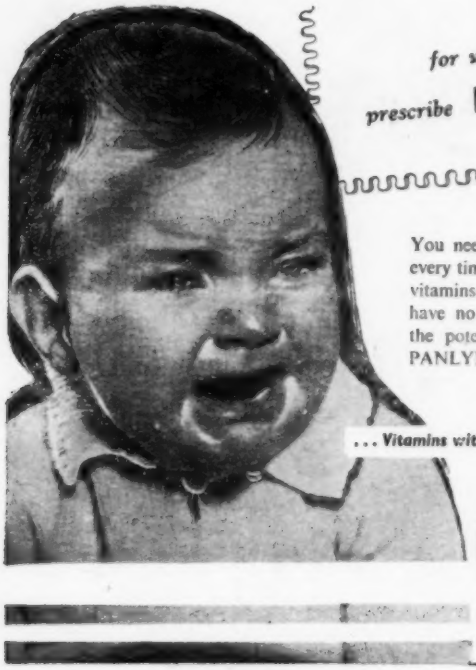

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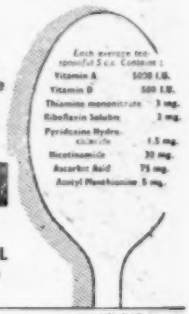
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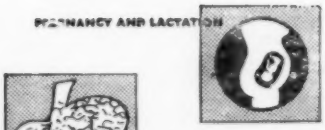

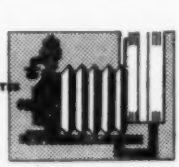

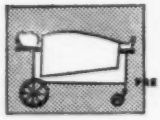

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